FACULTAD DE CIENCIAS MÉDICAS
"MIGUEL ENRÍQUEZ"

TESIS RESUMIDA EN POWERPOINT

"ADN MITOCONDRIAL

RELACIONADO A LA INFERTILIDAD POR EL VARICOCELE".

(HAPLOGRUPOS AFROAMERICANOS)

2005

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Objetivos

-La revisión actual se centra en la relación entre factores testiculares internos involucrados en daño en el ADN mitocondrial y su relación con el varicocele de 68 pacientes con infertilidad y de origen materno afroamericano.

- Confirmar la asociación entre los haplogrupos mitocondriales y la motilidad espermática.

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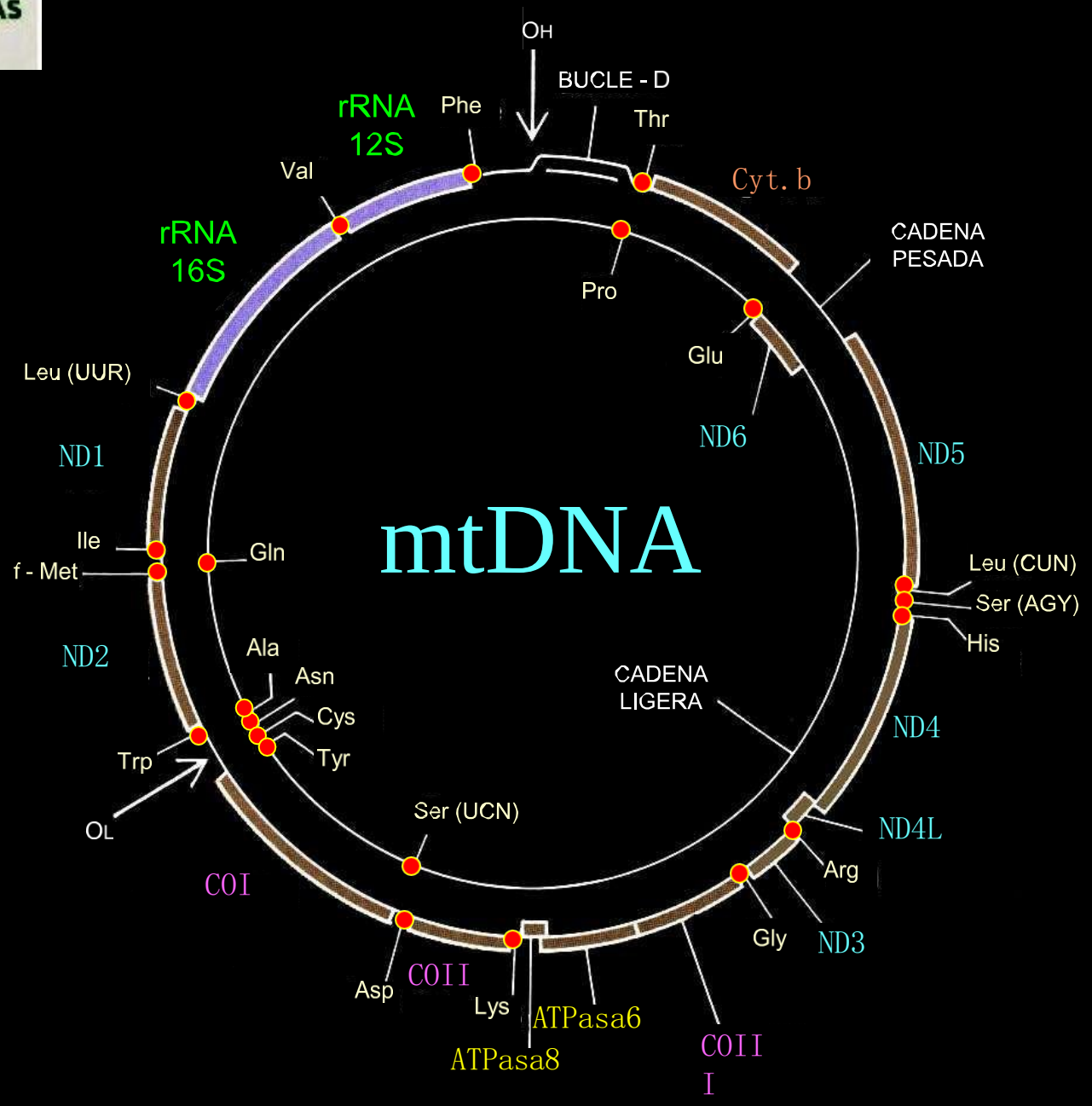

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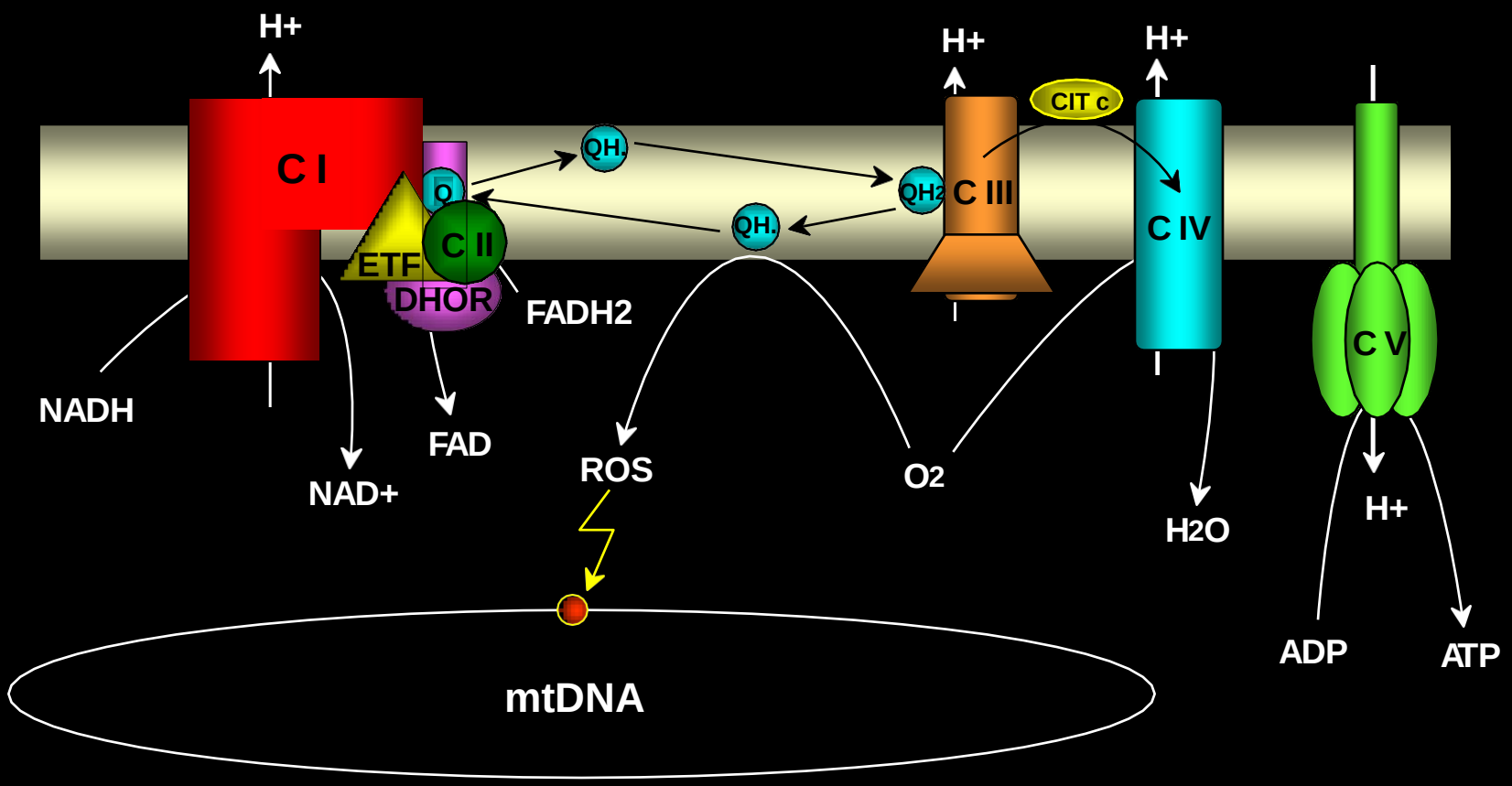
Cadena respiratoria



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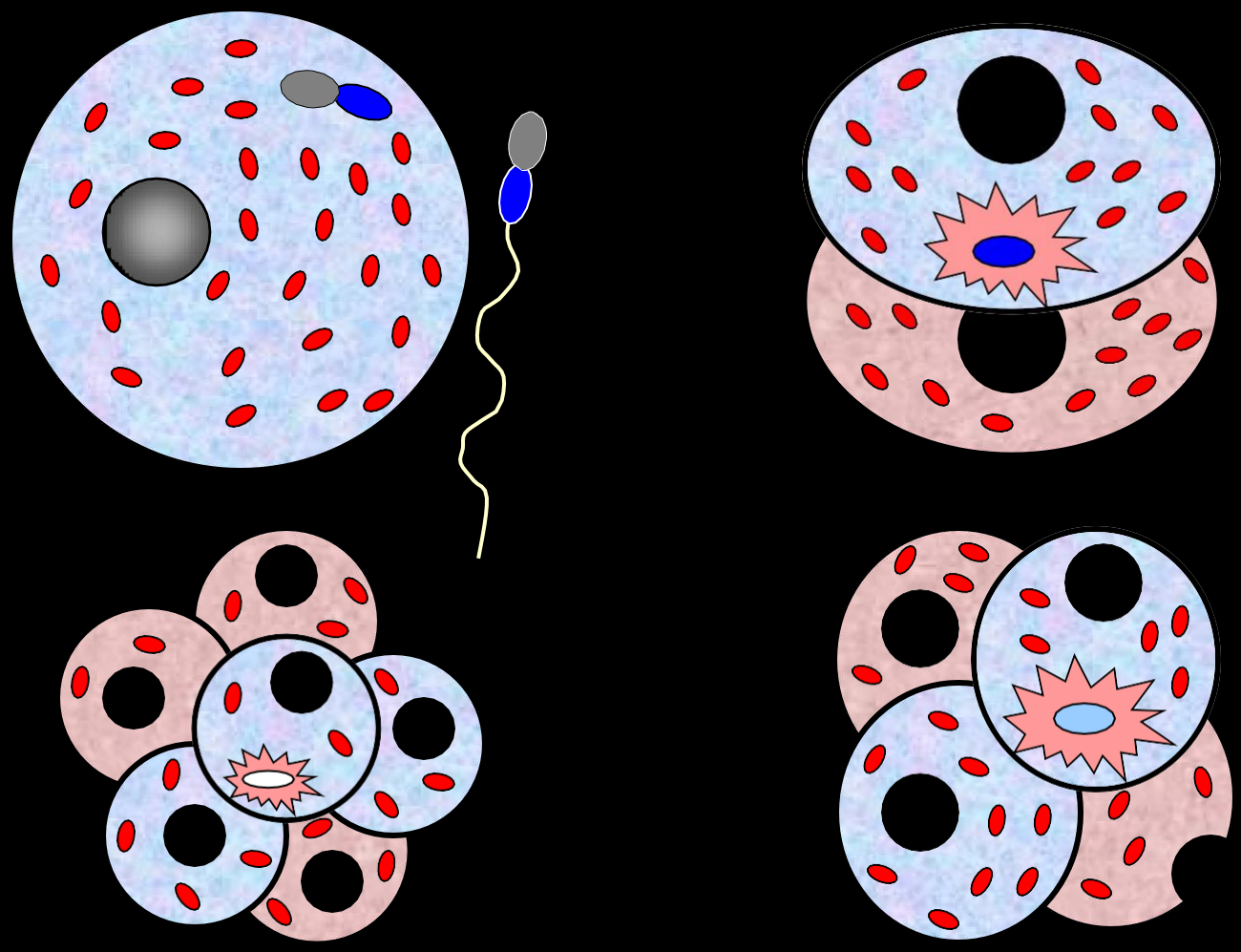
Herencia materna del mtDNA



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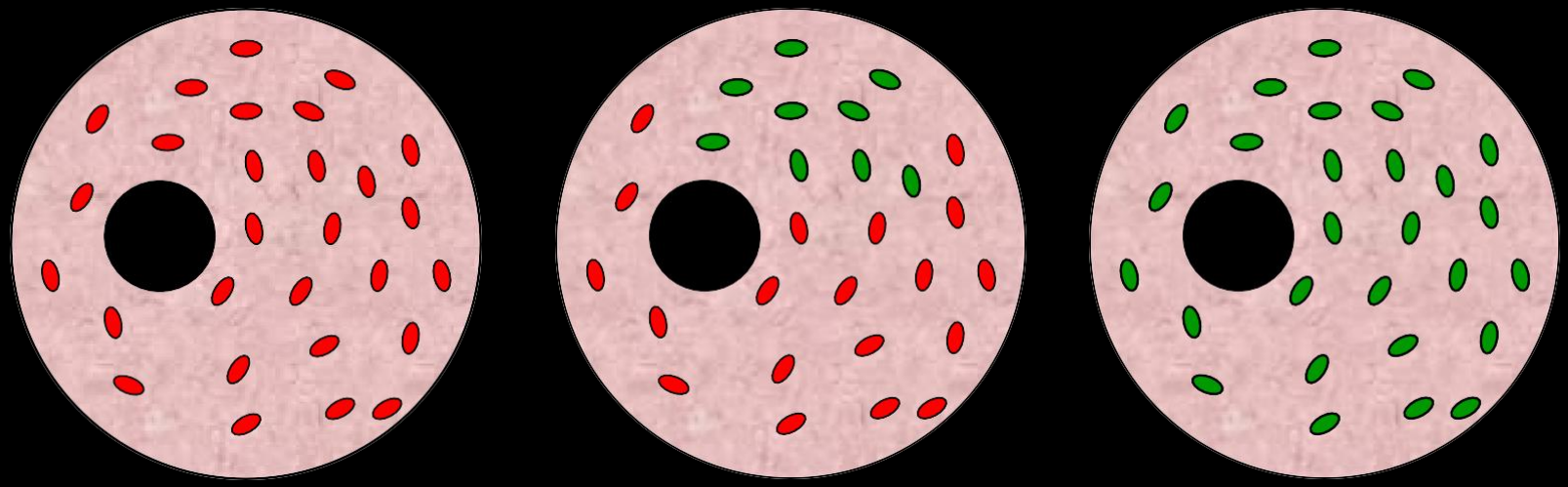
Homo / Heteroplasmia



HOMOPLASMIA HETEROPLASMIA HOMOPLASMIA

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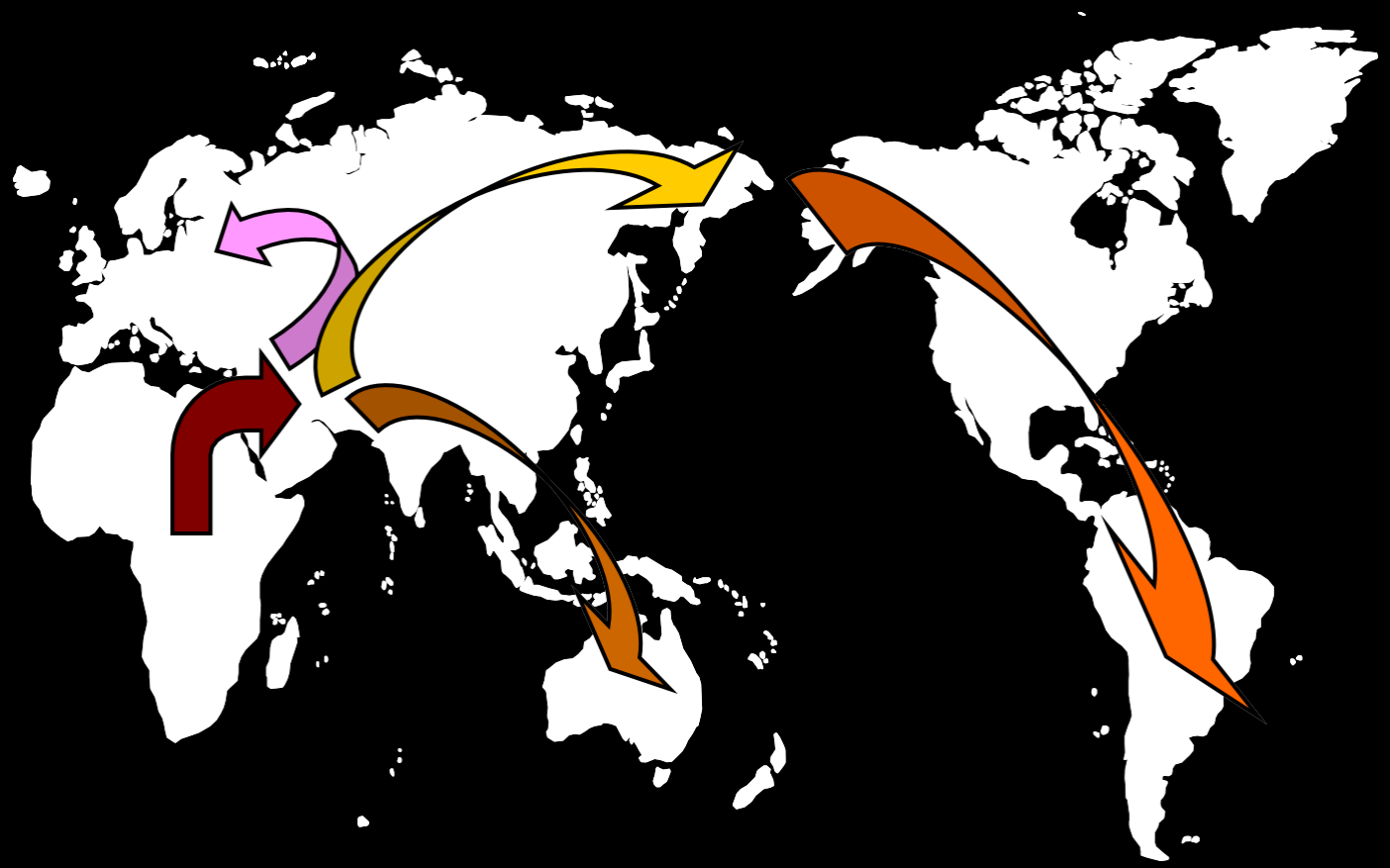
Origen africano y radiación continental



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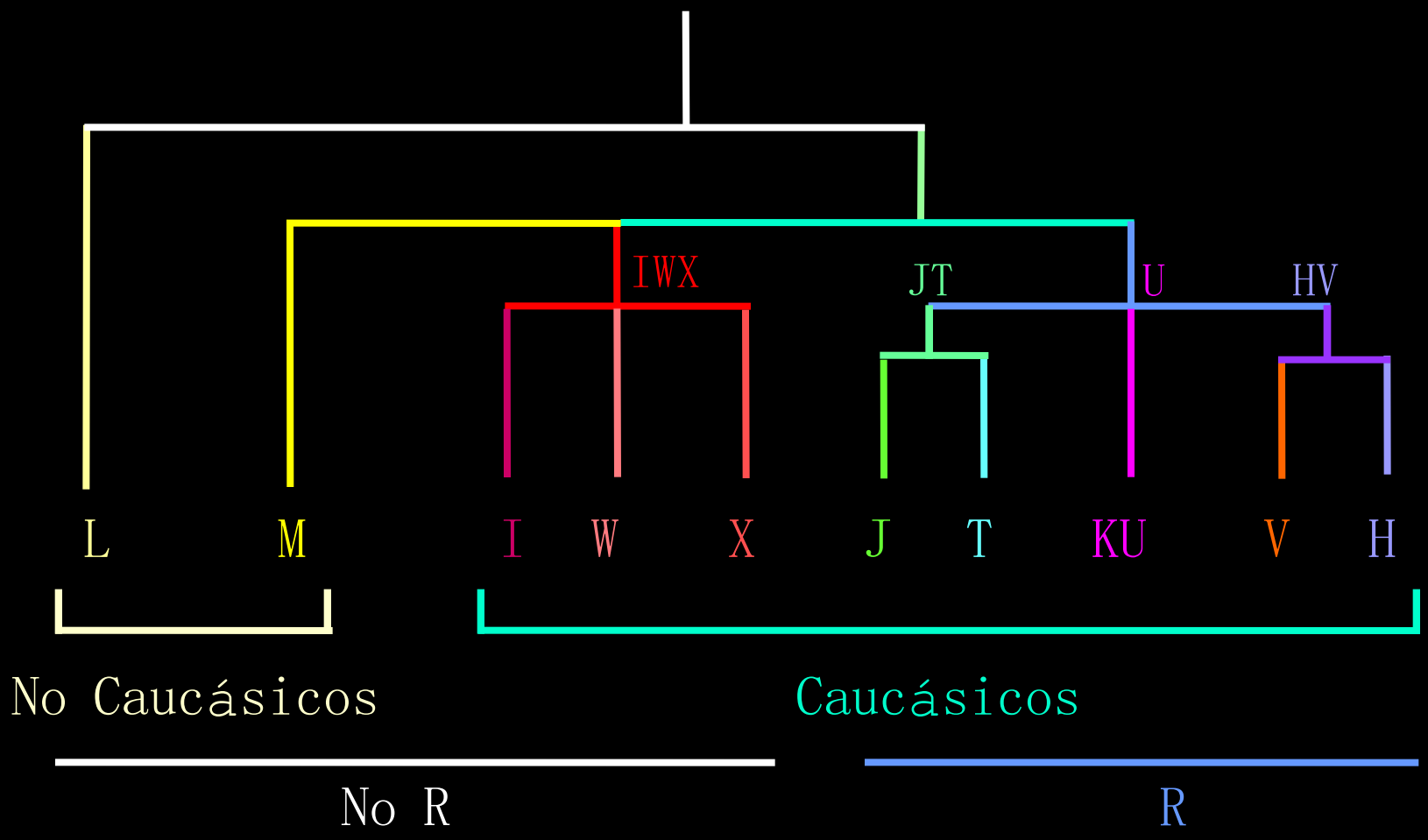
Filogenia del mtDNA



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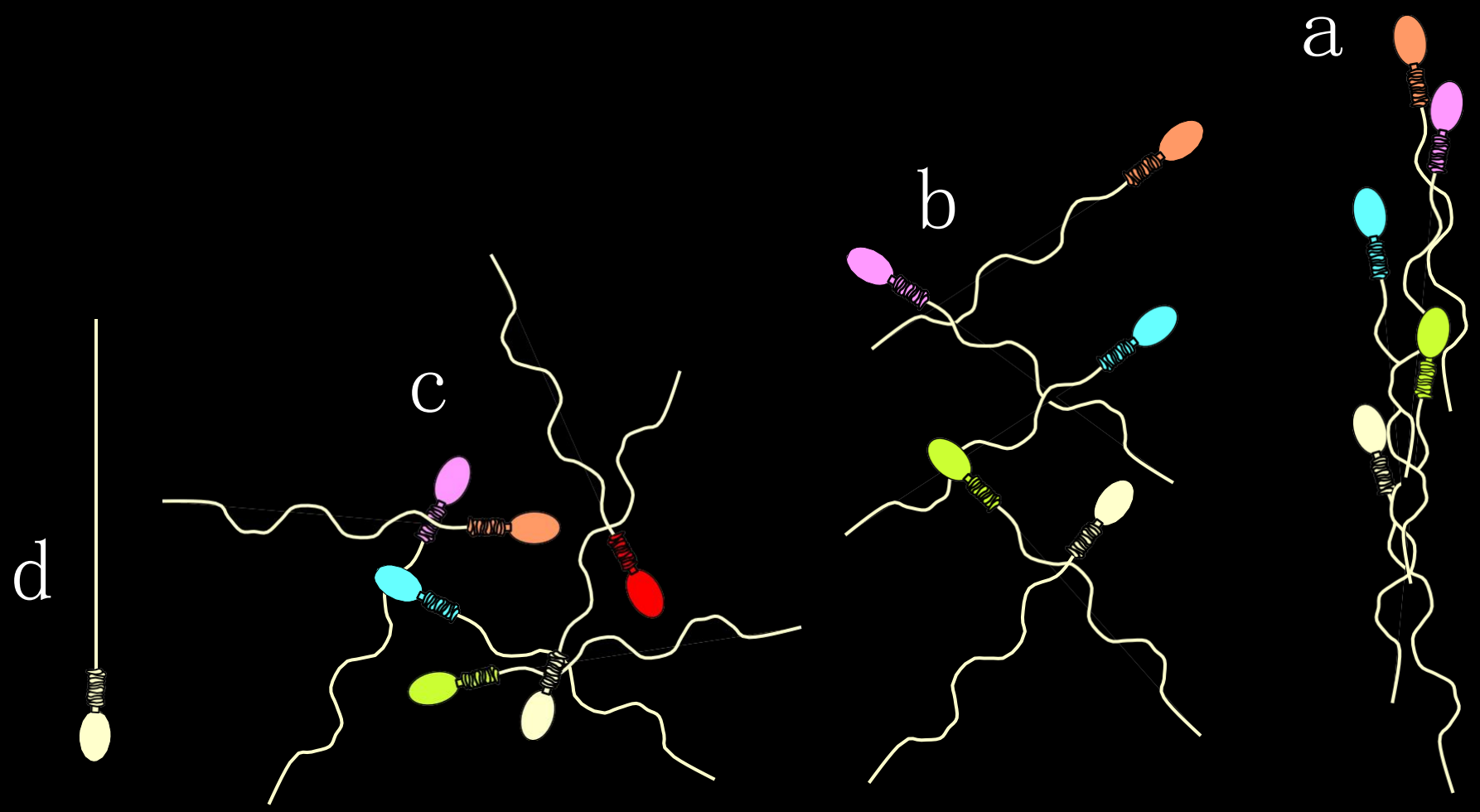
Motilidad espermática



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Genotipos mitocondriales vs fenotipos de motilidad

	GENOTIPOS MITOCONDRIALES	
FENOTIPO DE MOTILIDAD	LíNEAS FILOGENÉTICAS	HAPLOGRUPOS
CUALITATIVO	HV / MN; p = 0,002 JT / A; p = 0,032	H / MN; p = 0,002 T / A; p < 0,014
SEMICUANTITATIVO	HV / MN; p = 0,002 JT / AM; p < 0,001	H / MN; p = 0,002 T / AM; p < 0,001

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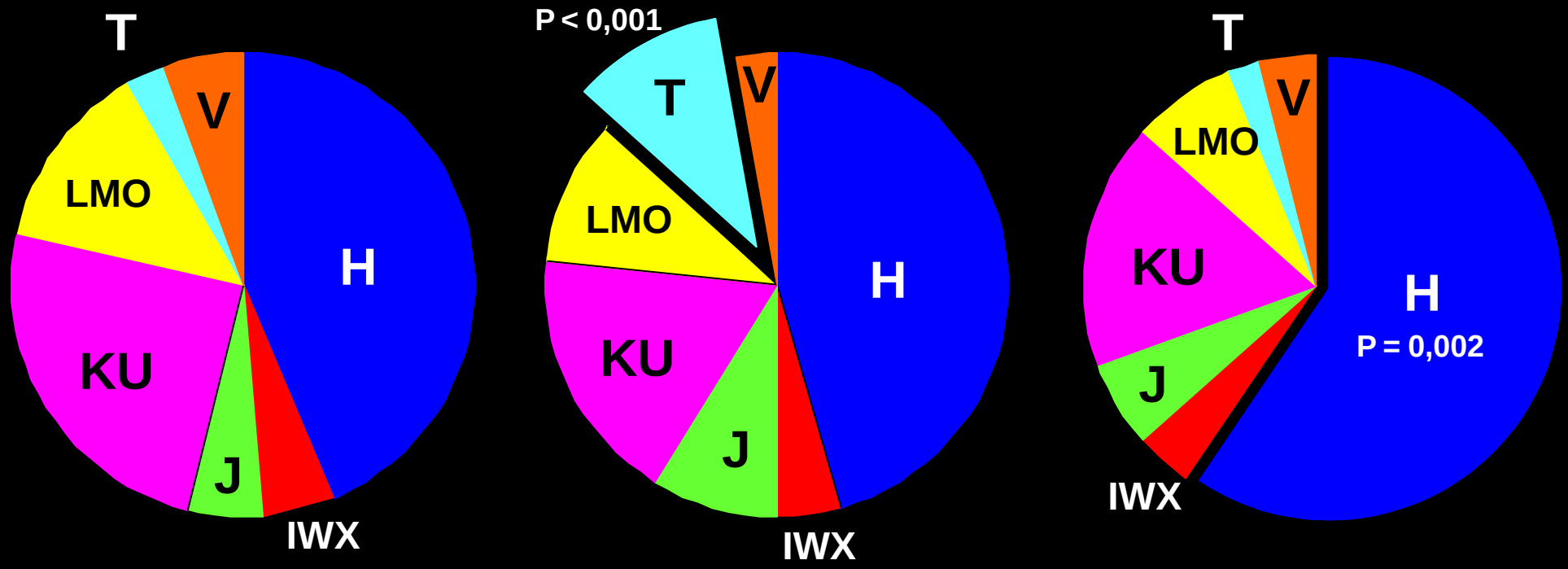
Haplogrupos mitocondriales vs motilidad espermática



ASTENOZOOSPERMIA SEVERA
< 25 %
(n = 146; 27 %)

ASTENOZOOSPERMIA MODERADA
50 % > AM ≥ 25 %
(n = 219; 40 %)

MOTILIDAD NORMAL
≥ 50 %
(n = 180; 33 %)

χ^2 = 29,1; DF = 12; p = 0,0038

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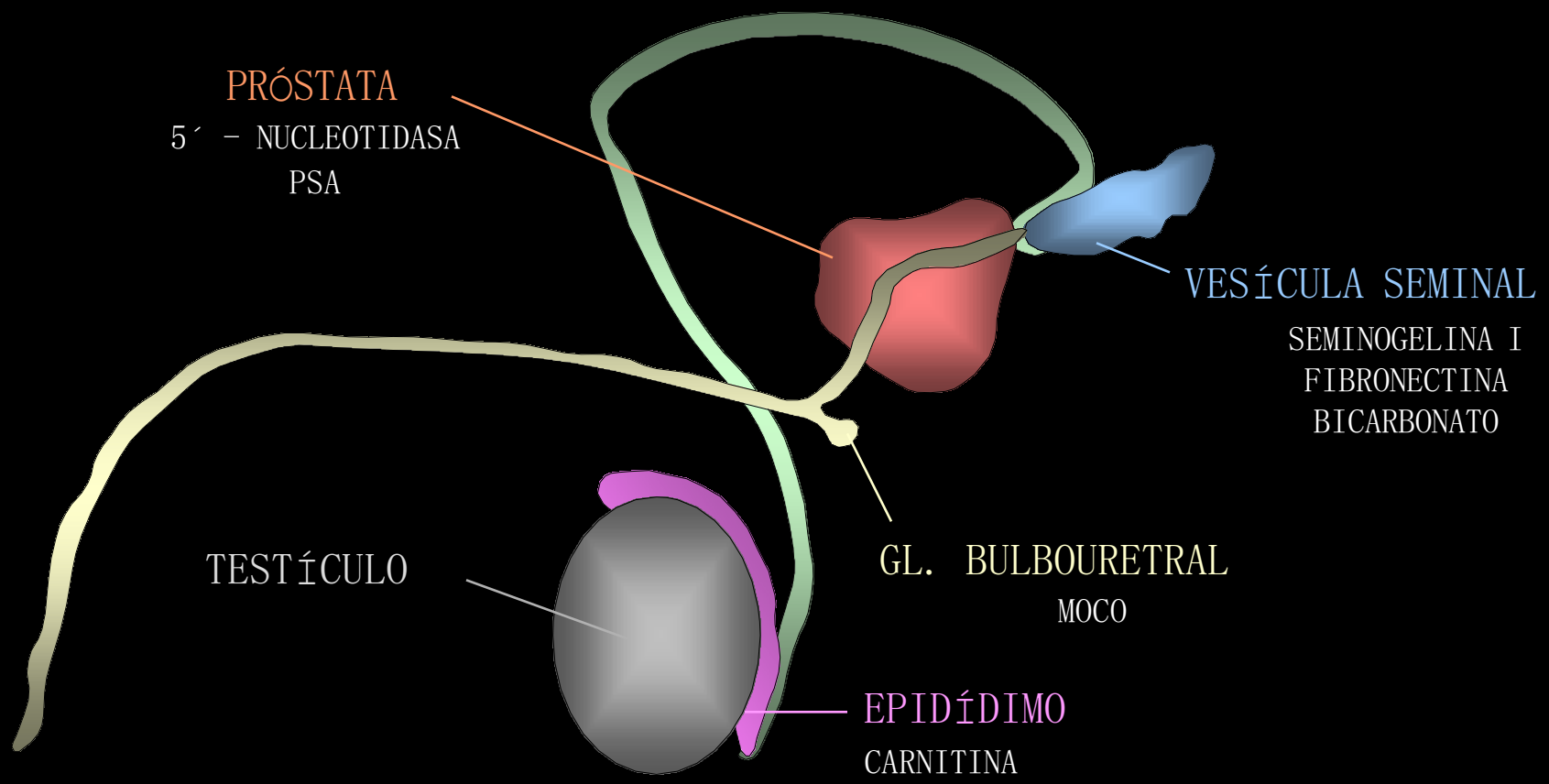
Sistema reproductor masculino



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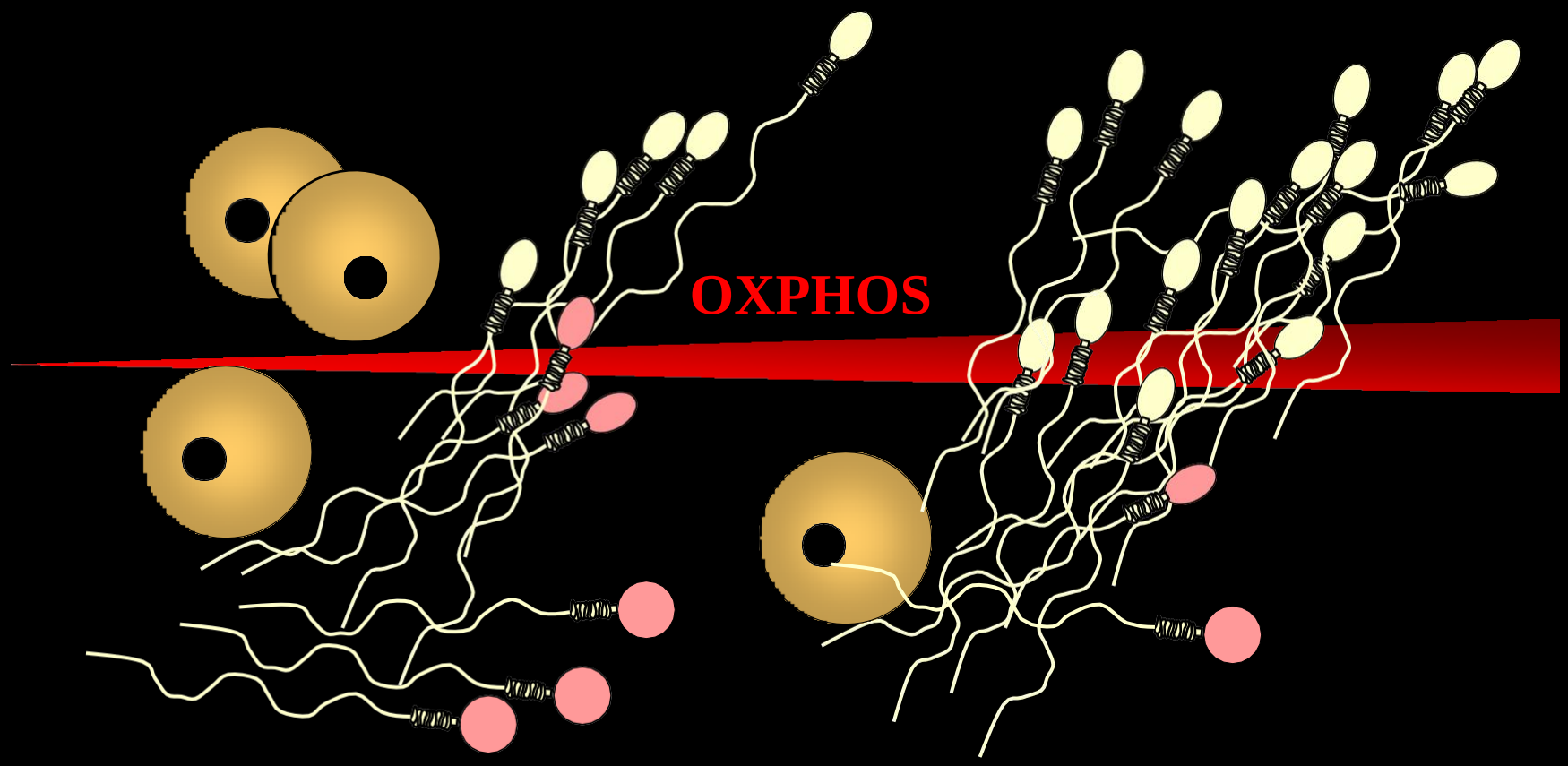
Calidad seminal y diferenciación mitocondrial



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Marcadores de función reproductora

VARIABLES PREANALÍTICAS
- Edad
- Retardo preanalítico

GLÁNDULAS SEXUALES ACCESORIAS
- PRÓSTATA
  - Calcio
  - Magnesio
  - Zinc
  - Citrato
- VESÍCULAS SEMINALES
  - Fructosa
- EPIDÍDIMO
  - Carnitina

Volumen
pH

PARÁMETROS ESPERMATOGÉNICOS
- Conc de espermatozoides
- Conc de células redondas
- % espermatozoides vitales
- % espermatozoides anormales

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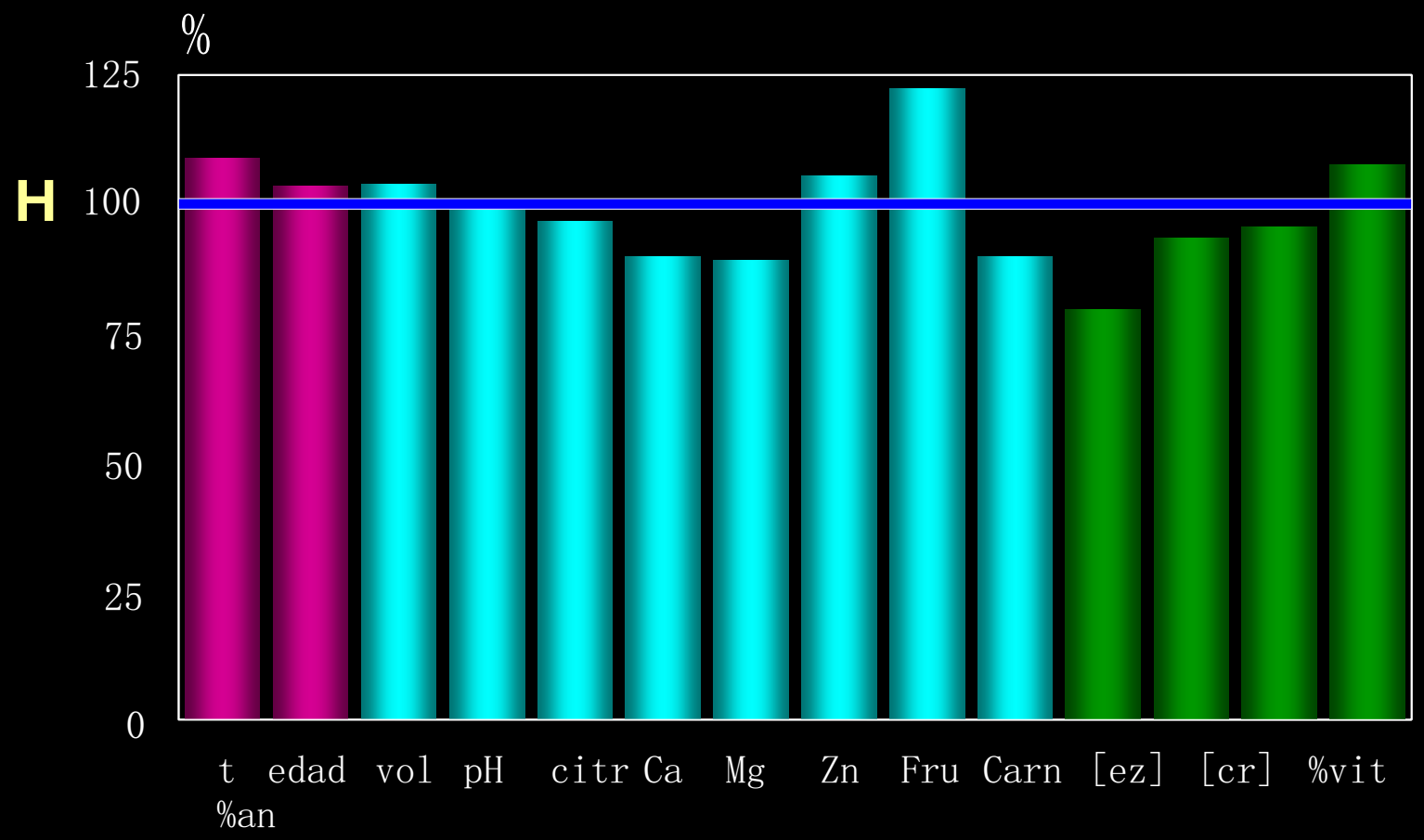
Marcadores de función reproductora en los haplogrupos H y T



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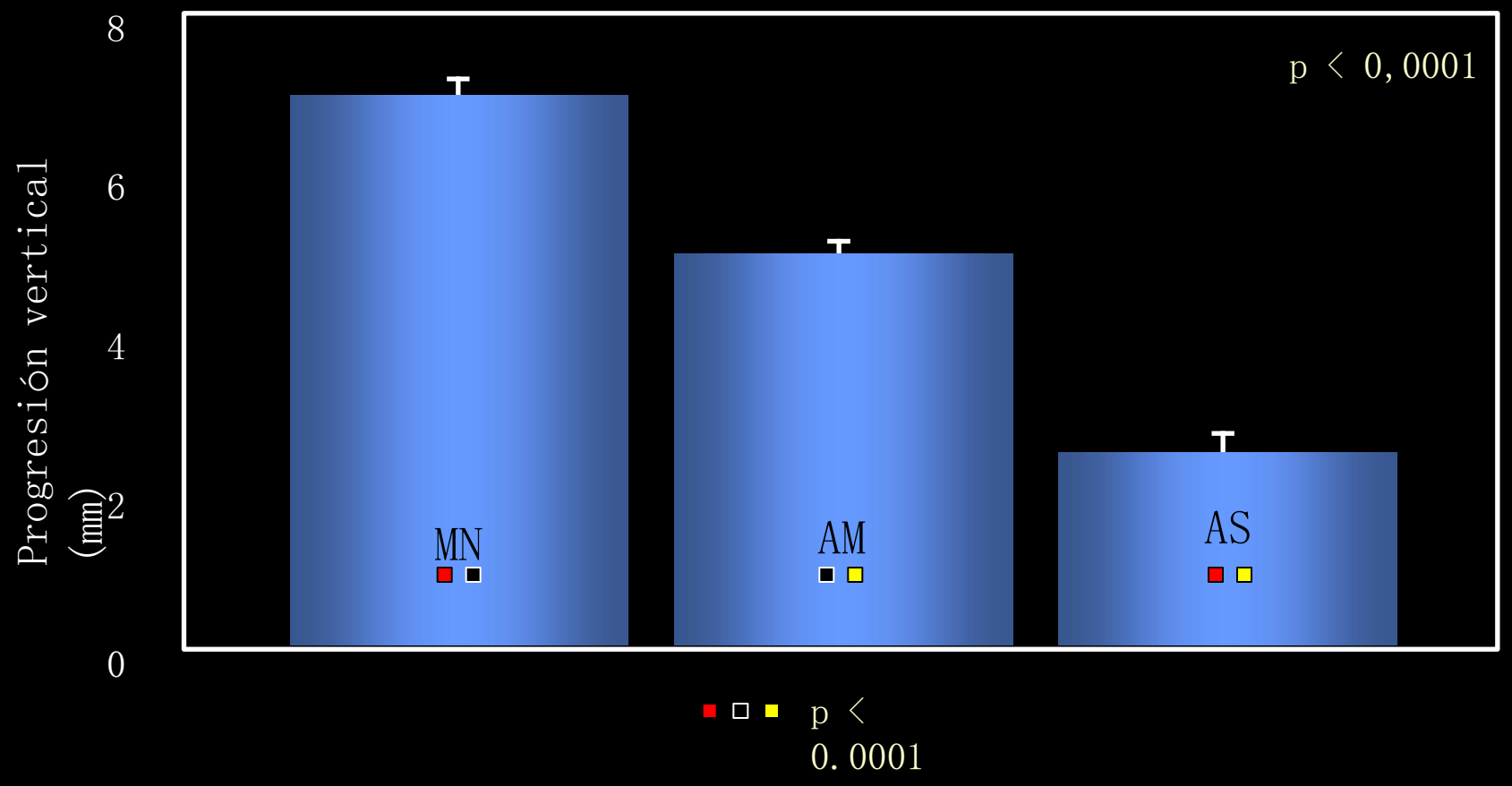
Progresión vertical vs fenotipos de motilidad



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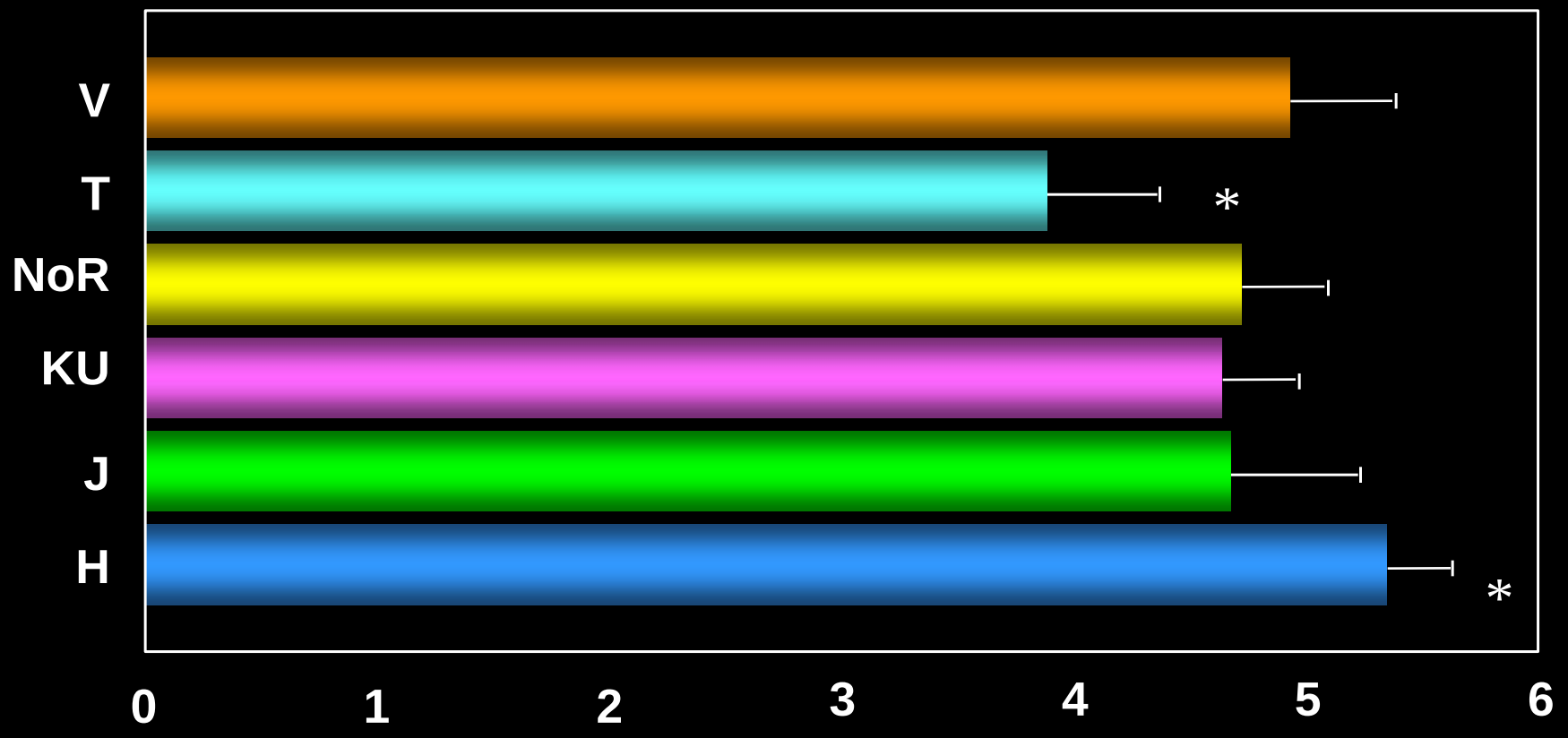
Haplogrupos mitocondriales vs progresión vertical



*; p = 0,0287

CONCLUSIONES:

HAY ASOCIACIÓN ENTRE LOS HAPLOGRUPOS MITOCONDRIALES Y LA MOTILIDAD ESPERMÁTICA. EL HAPLOGRUPO H CONFIERE RESISTENCIA A LA ASTENOZOOSPERMIA.

EL HAPLOGRUPO T CONFIERE SUSCEPTIBILIDAD A LA ASTENOZOOSPERMIA.

CONCLUSIONES:

EL HAPLOGRUPO T CUBANO ES REPRESENTATIVO DEL HAPLOGRUPO T AFROAMERICANO.

ES EL CONJUNTO DEL HAPLOGRUPO T, Y NO UNA RAMA PARTICULAR, EL ASOCIADO A LA ASTENOZOOSPERMIA MODERADA.

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CONCLUSIONES:

LA DISTRIBUCIóN DE LOS HAPLOGRUPOS MITOCONDRIALES EN LA POBLACÍóN CUBANA ES REPRESENTATIVA DE LA POBLACIóN AFROAMERICANA GENERAL.

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Estudio del fenotipo bioquímico

CONCLUSIONES:

EN LOS 68 PACIENTES CON DIFERENTES GRADOS DE VARICOCELE:

-SE CONFIRMÓ LA ASOCIACIÓN ENTRE EL ADN mitocondrial Y LA MOTILIDAD ESPERMÁTICA.

- EL FENOTIPO BIOQUÍMICO QUE ASOCIA LA MOTILIDAD ESPERMÁTICA AL FONDO GENÉTICO MITOCONDRIAL ES LA FUNCIÓN RESPIRATORIA.

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Estudio del fenotipo molecular

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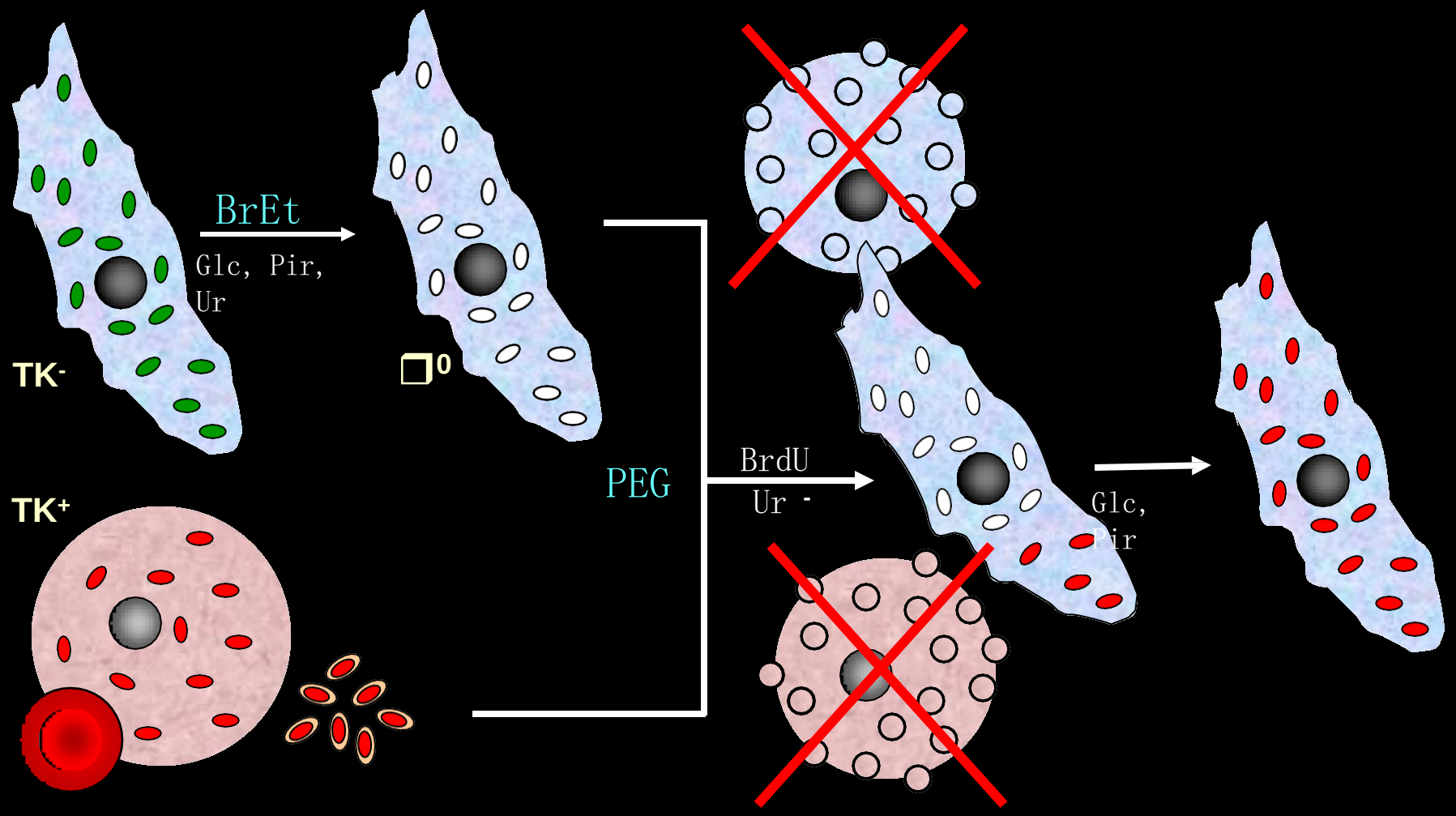
Cíbridos



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Condiciones de estrés

ESTADO	TEMPERATURA	FUENTE ENERGÉTICA
BASAL	37 ° C	GLUCOSA
ESTRÉS BAJO	35 ° C	GLUCOSA
ESTRÉS MODERADO	37 ° C	GALACTOSA
ESTRÉS SEVERO	35 ° C	GALACTOSA

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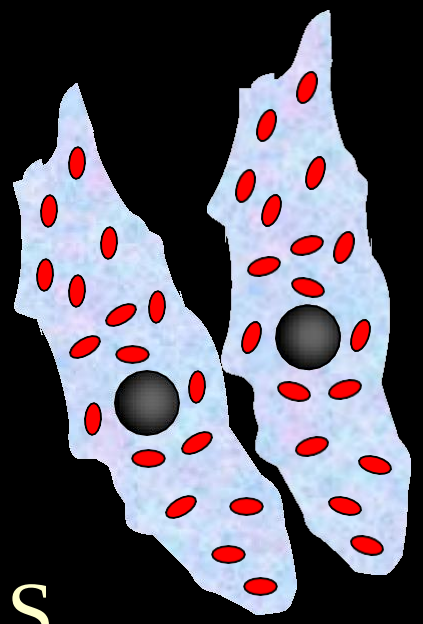
Estrés y biogénesis mitocondrial

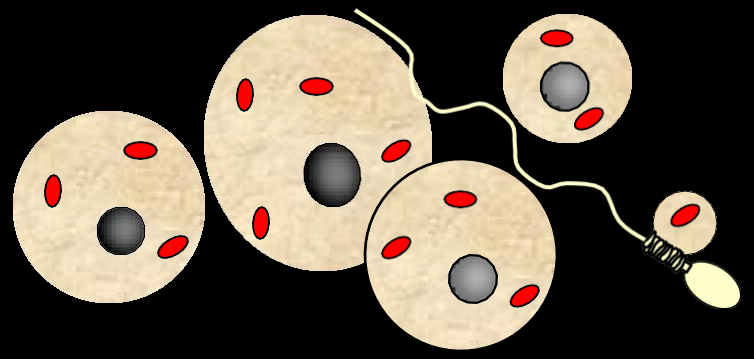
CULTIVO CELULAR

BIOGÉNESIS MITOCONDRIAL

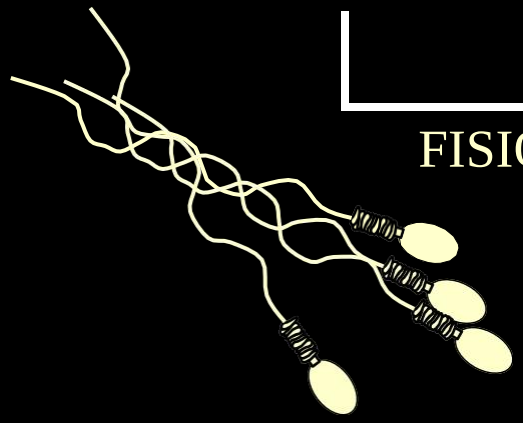
EXPERIMENTAL



ESTRÉS



ESPERMATOGÉNESIS



FISIOLÓGICO

NO BIOGÉNESIS MITOCONDRIAL

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RECOMENDACIONES.

-Sugerimos que se realice la reparación del varicocele en pacientes que tienen alta fragmentación de ADN mitocondrial asociado a la infertilidad masculina en sus muestras de semen antes de la cirugía.

- Se recomienda un control anual con ultrasonidos del volumen testicular, ya que es el método más preciso y reproducible para medir las variaciones en el tamaño del testículo.

-Variaciones de más de 2 ml o del 20% del volumen por ecografía es actualmente el mejor indicador de daño testicular.

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Summary Thesis in PowerPoint

Mitochondrial DNA

RELATED TO INFERTILITY DUE TO VARICOCELE".

(AFROAMERICAN HAPLOGROUPS)

2005

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Objectives

-The current review focuses on the relationship between testicular factors internal involved in DNA damage mitochondrial and its relationship with the varicocele of 68 patients with infertility and of African-American maternal origin.

- Confirm the association between the Mitochondrial haplogroups and motility spermatic

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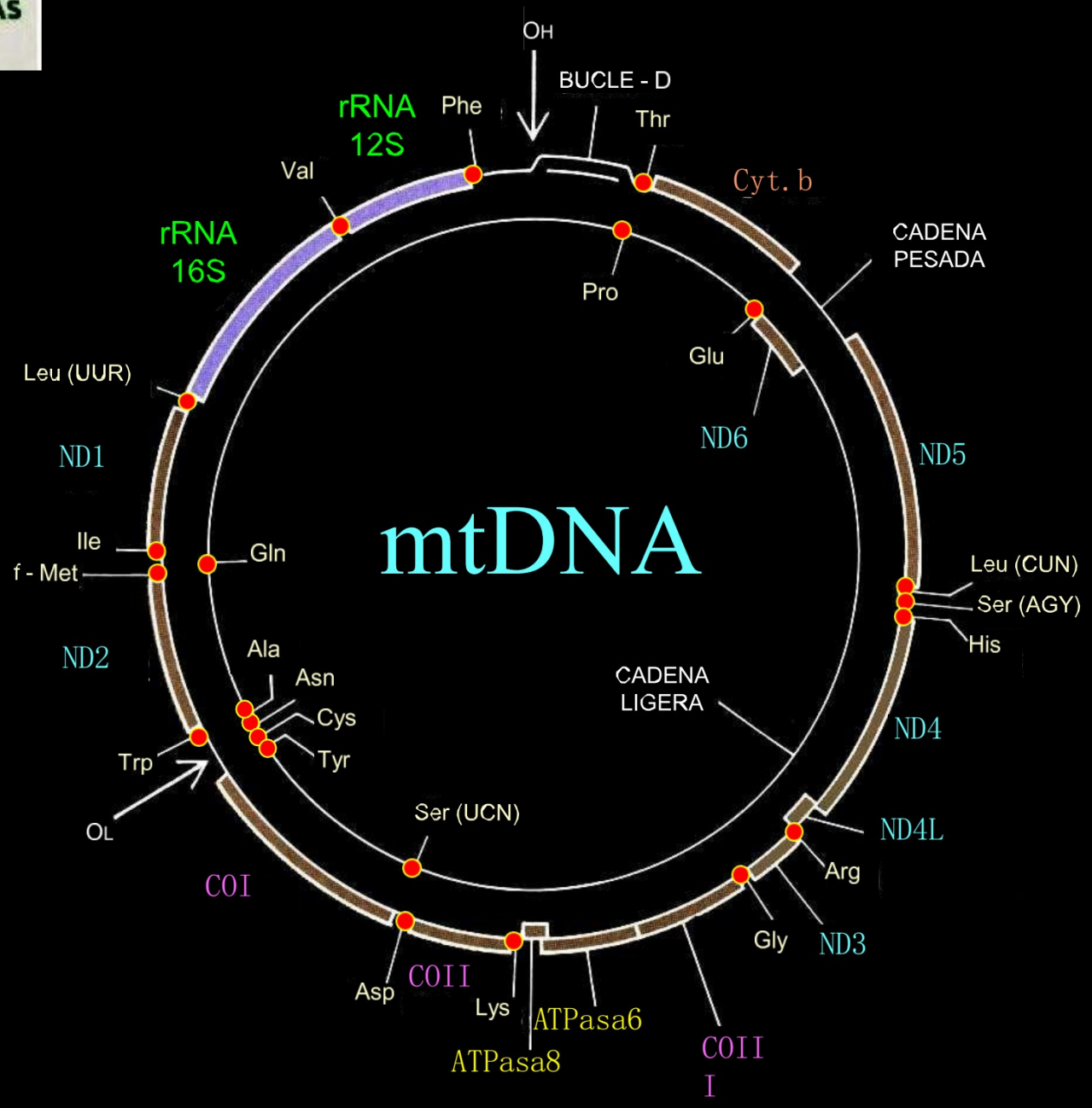

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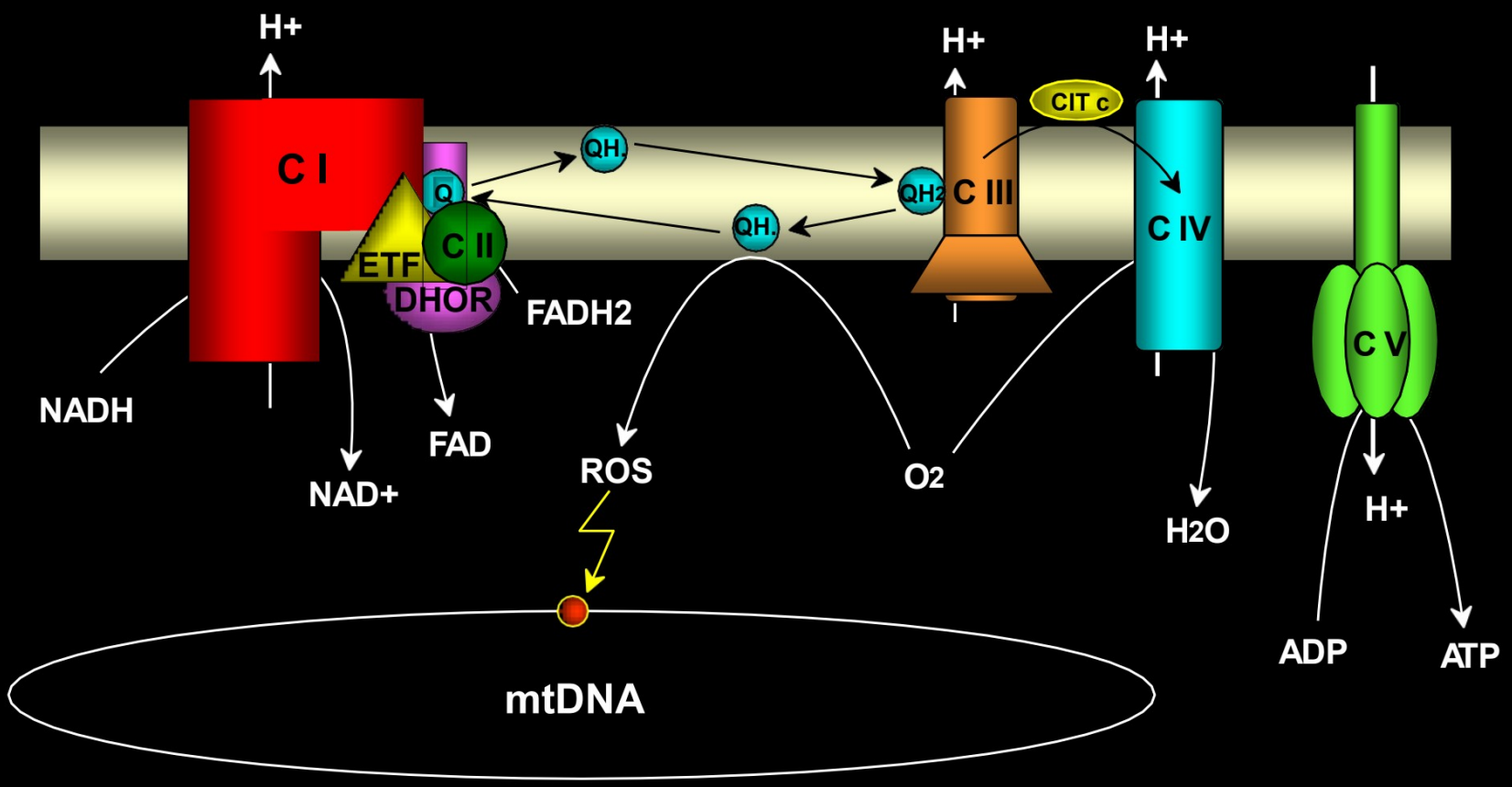
Cadena respiratoria



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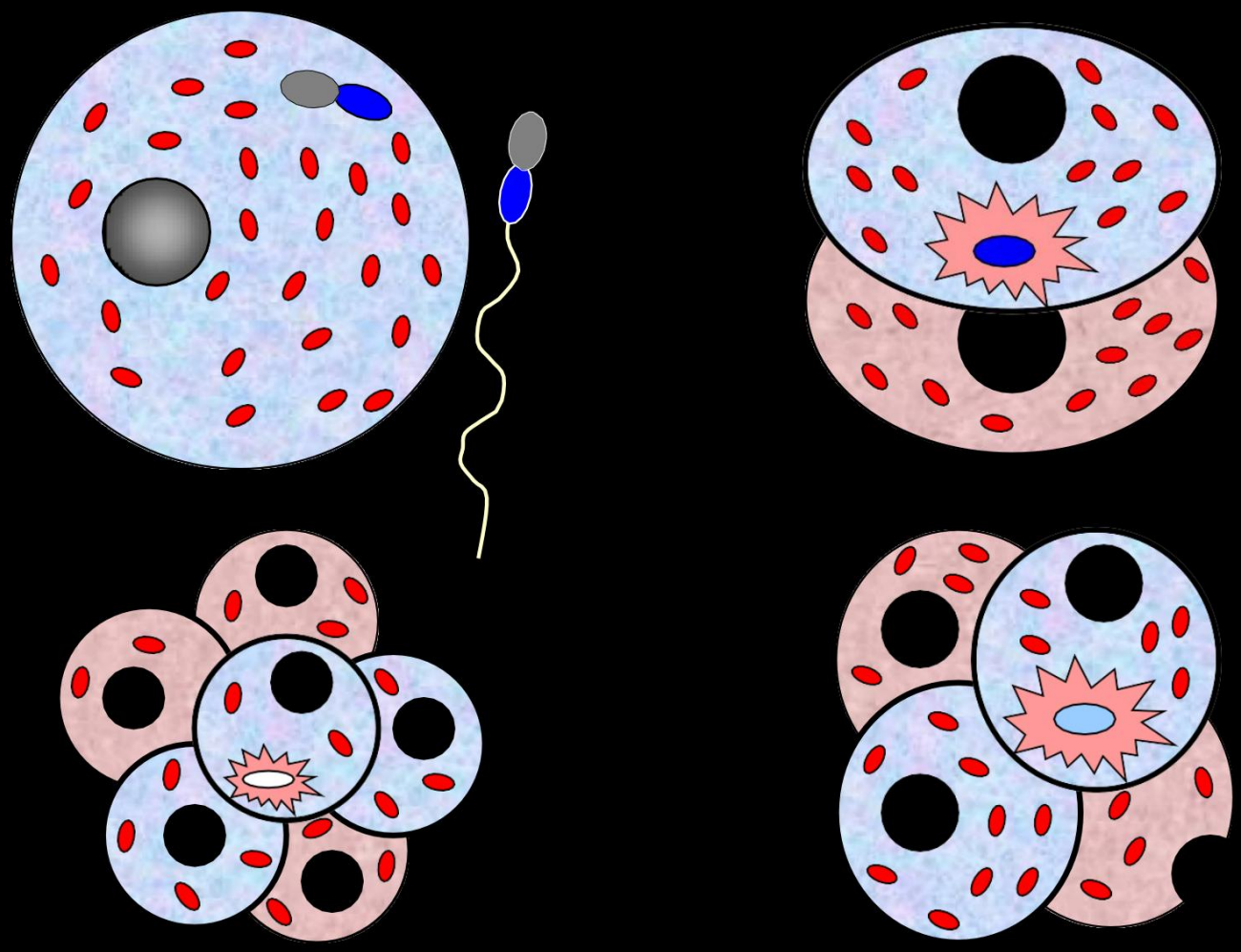
Maternal inheritance of mtDNA



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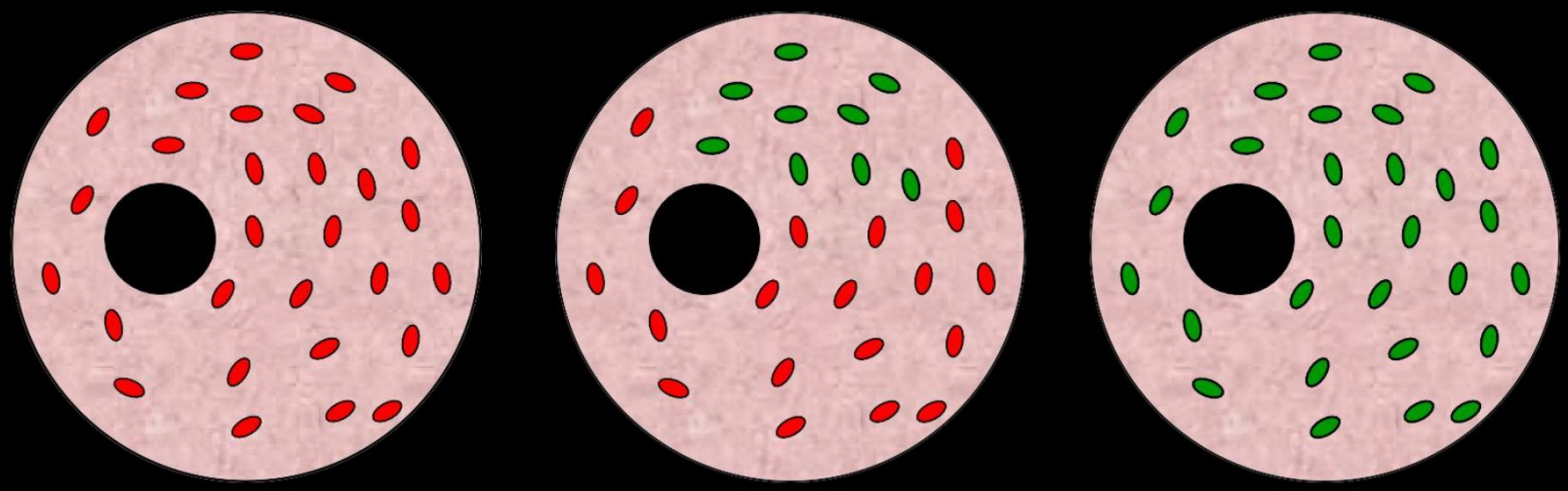
Homo/Heteroplasmy



HOMOPLASMY HETEROPLASMIA HOMOPLASMY

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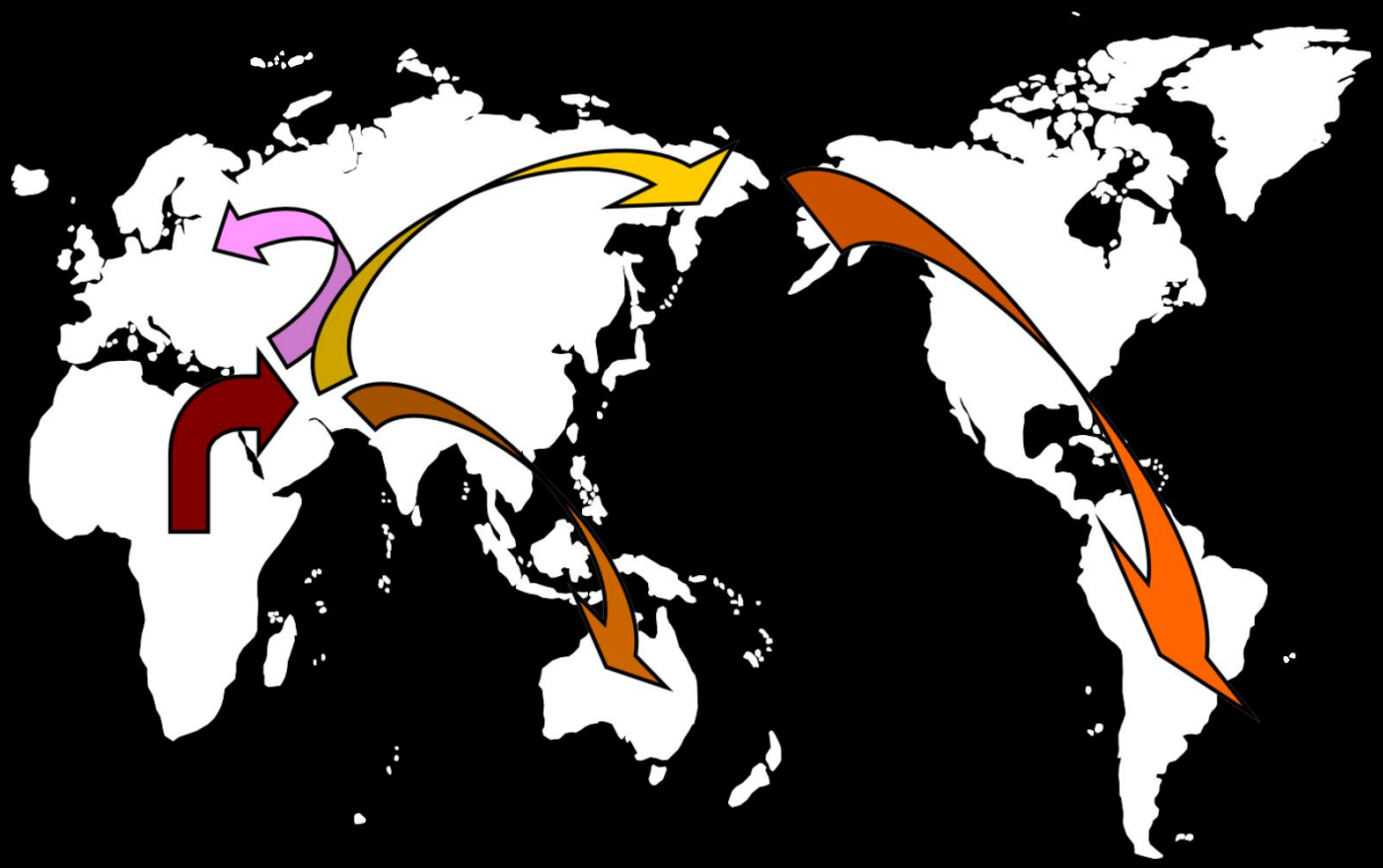
African origin and continental radiation



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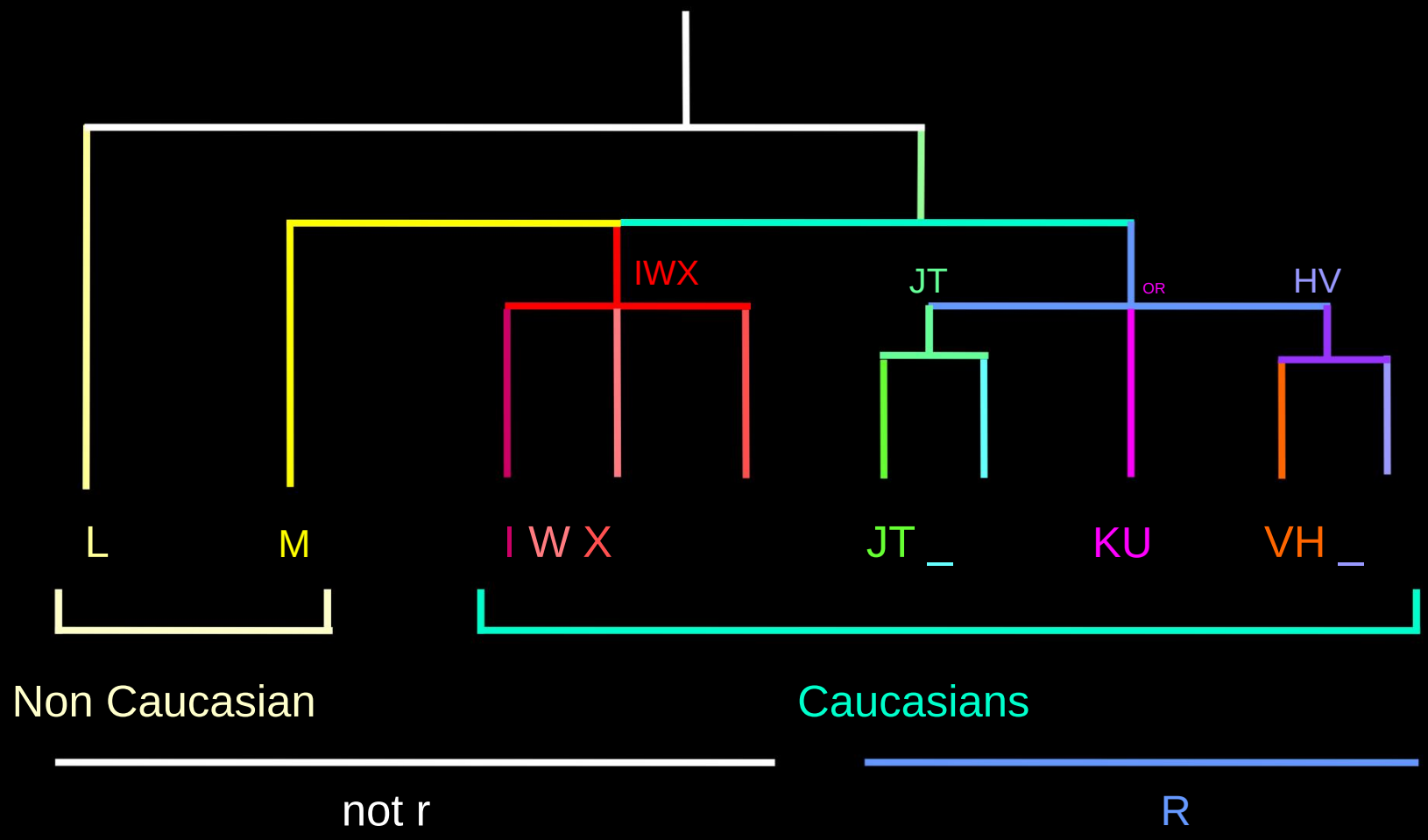
mtDNA phylogeny



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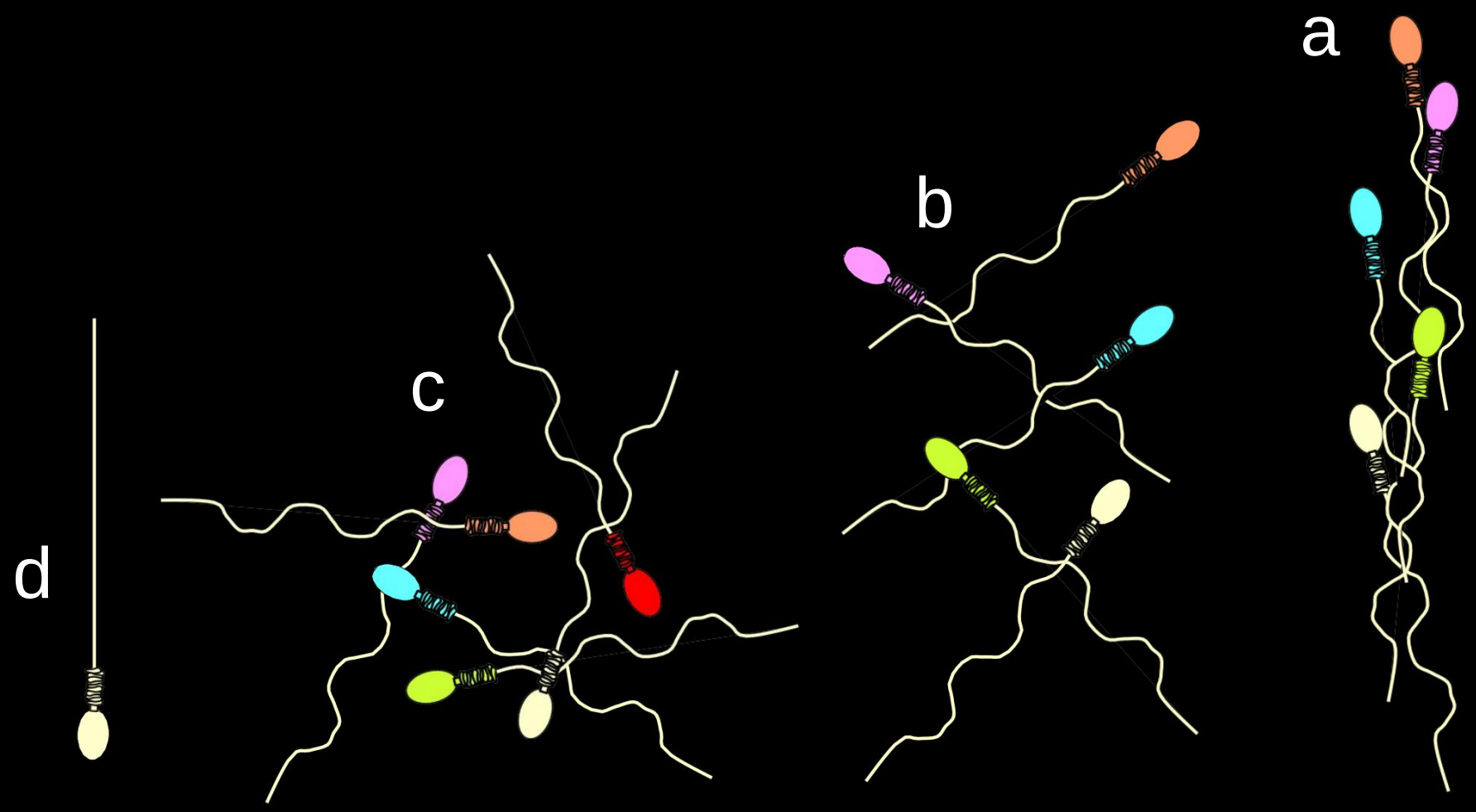
Sperm motility



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Mitochondrial genotypes vs motility phenotypes

PHENOTYPE OF MOTILITY	MITOCHONDRIAL GENOTYPES: LINES PHYLOGENETICS	MITOCHONDRIAL GENOTYPES: HAPLOGROUPS
QUALITATIVE	HV/MN; p = 0.002 JT/A; p = 0.032	H/MN; p = 0.002 T/A; p < 0.014
SEMI-QUANTITATIVE	HV/MN; p = 0.002 JT/AM; p < 0.001	H/MN; p = 0.002T/AM; p < 0.001

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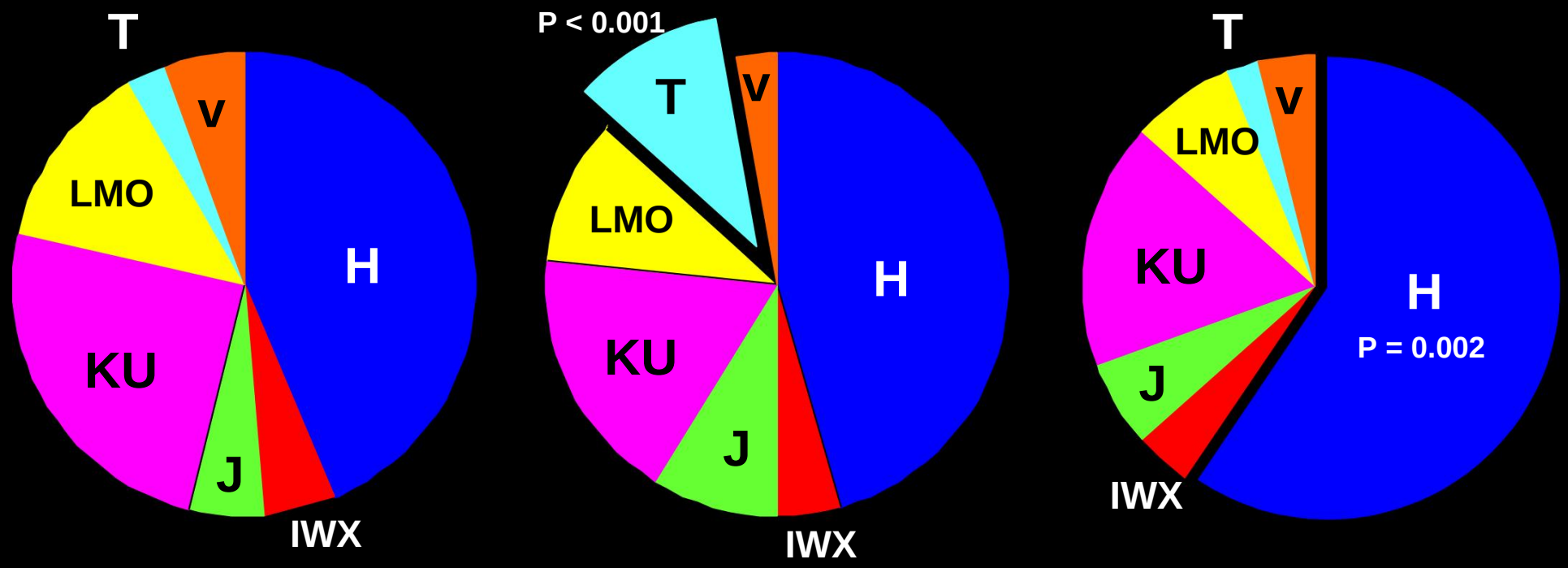
Mitochondrial haplogroups vs sperm motility



ASTHENOZOOSPERMIA SEVERE	ASTHENOZOOSPERMIA MODERATE	MOTILITY NORMAL
< 25%	50% > AM ÿ 25%	ÿ 50%
(n=146; 27%)	(n=219; 40%)	(n=180; 33%)

ÿ2 = 29.1; DF = 12; p = 0.0038

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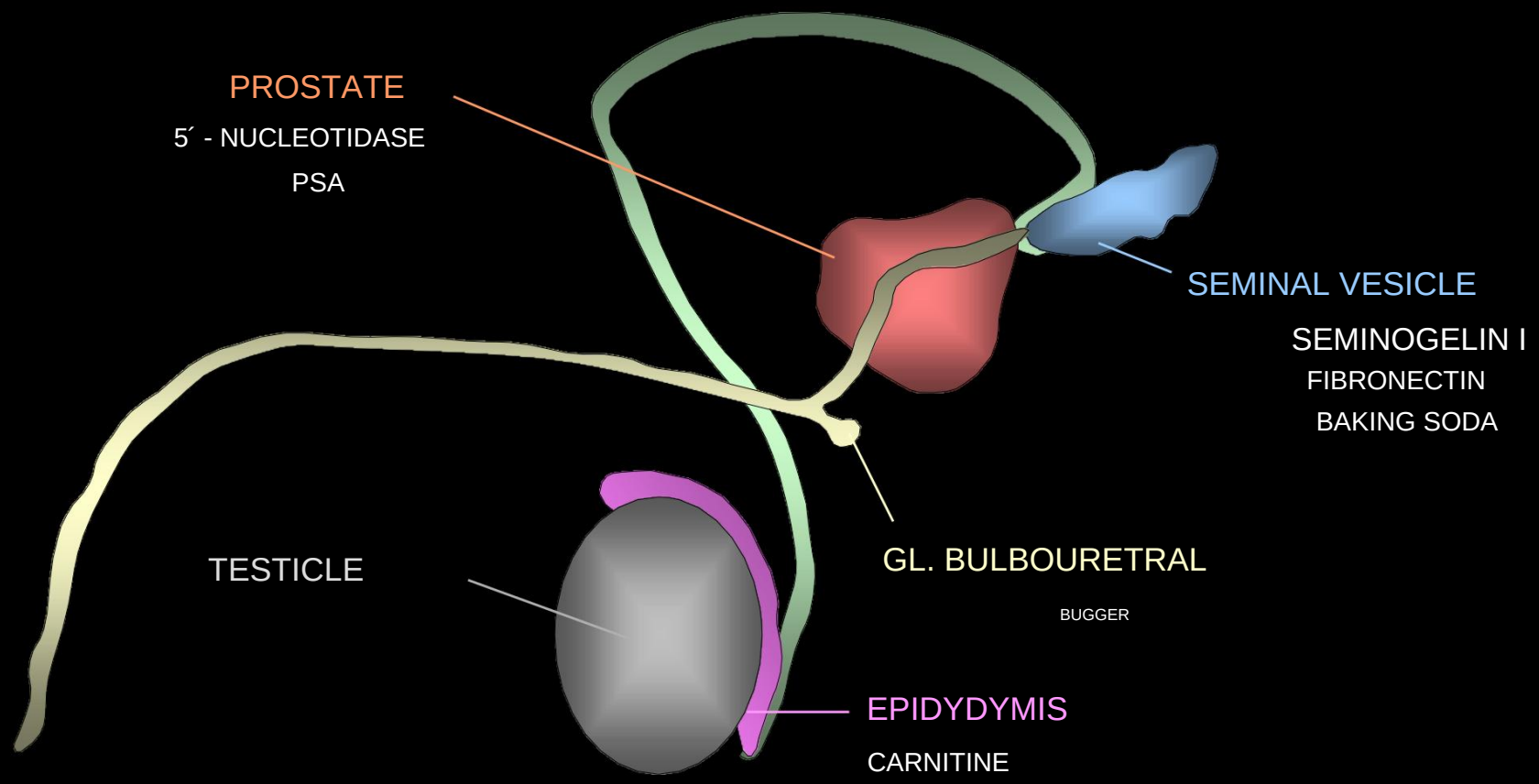
Male reproductive system



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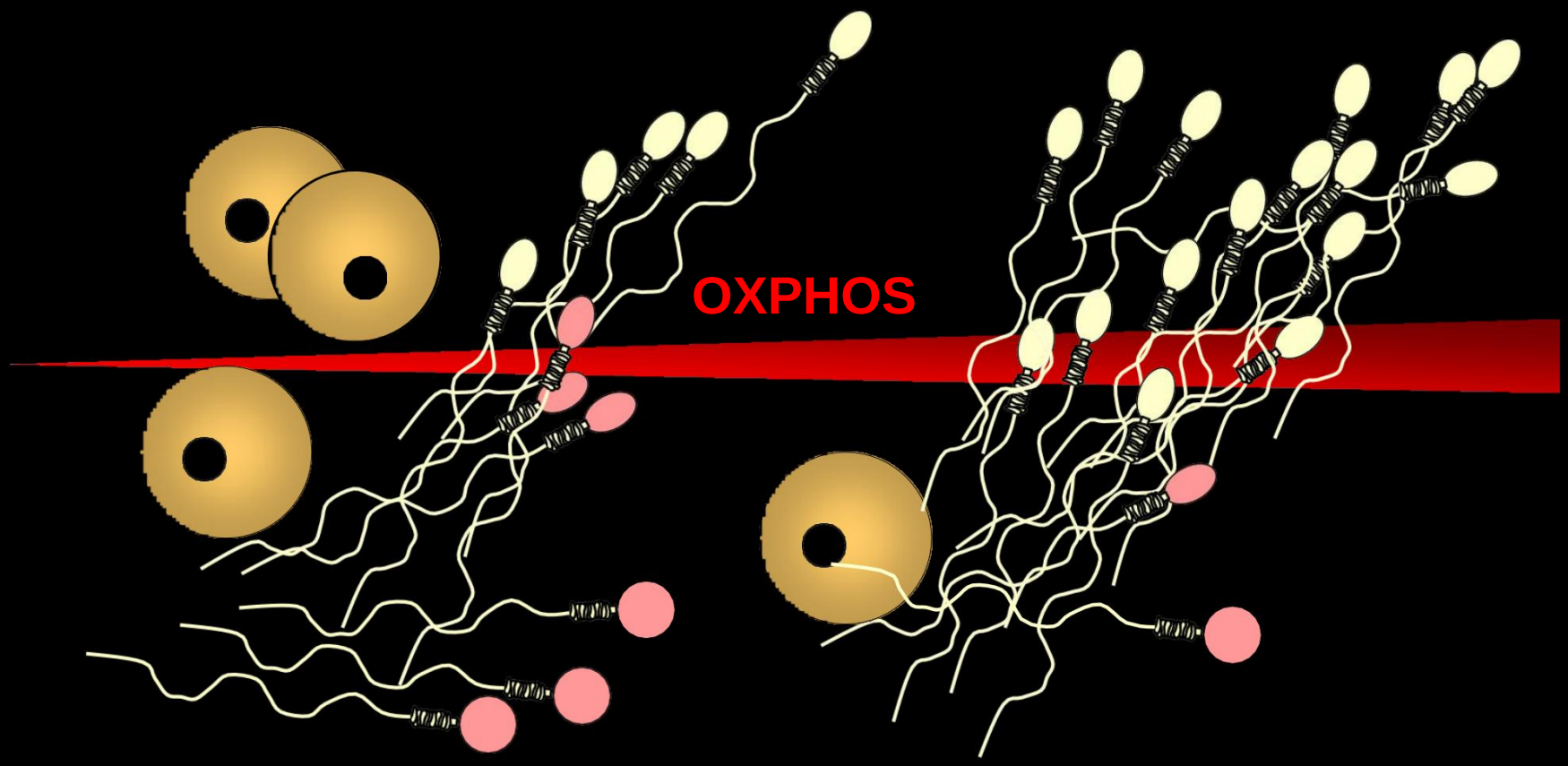
Seminal quality and mitochondrial differentiation



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Reproductive function markers

VARIABLES PREANALYTICS

- Age
- Preanalytical delay

GLANDS SEXUAL ACCESSORIES

- PROSTATE
  - Calcium
  - Magnesium
  - Zinc
  - Citrate
- SEMINAL VESICLES
  - Fructose
- EPIDYDYMIS
  - carnitine

volume

pH

PARAMETERS SPERMATOGENIC

- sperm conc
- round cell conc
- % vital sperm
- % abnormal sperm

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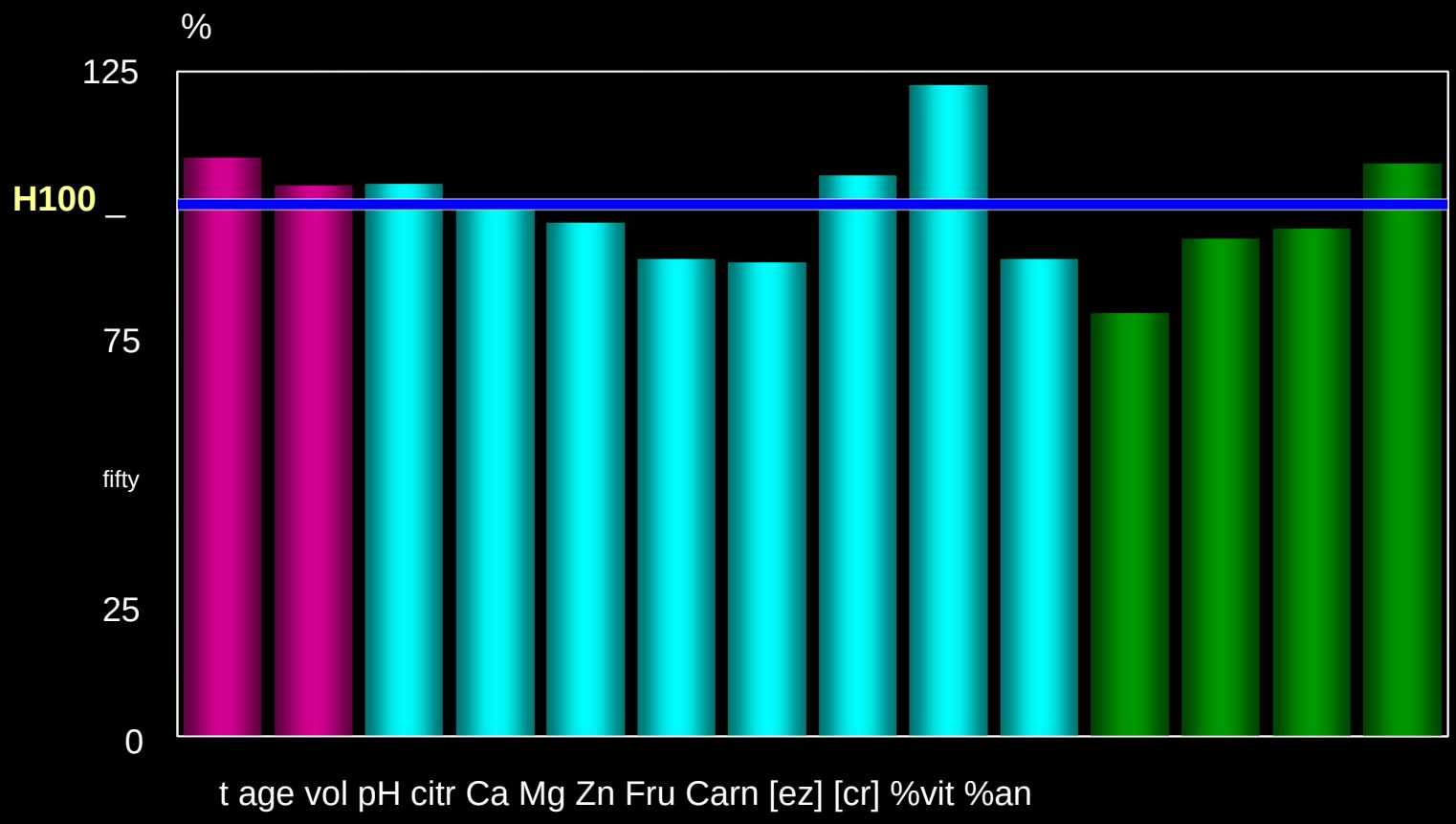
Reproductive function markers in haplogroups H and T



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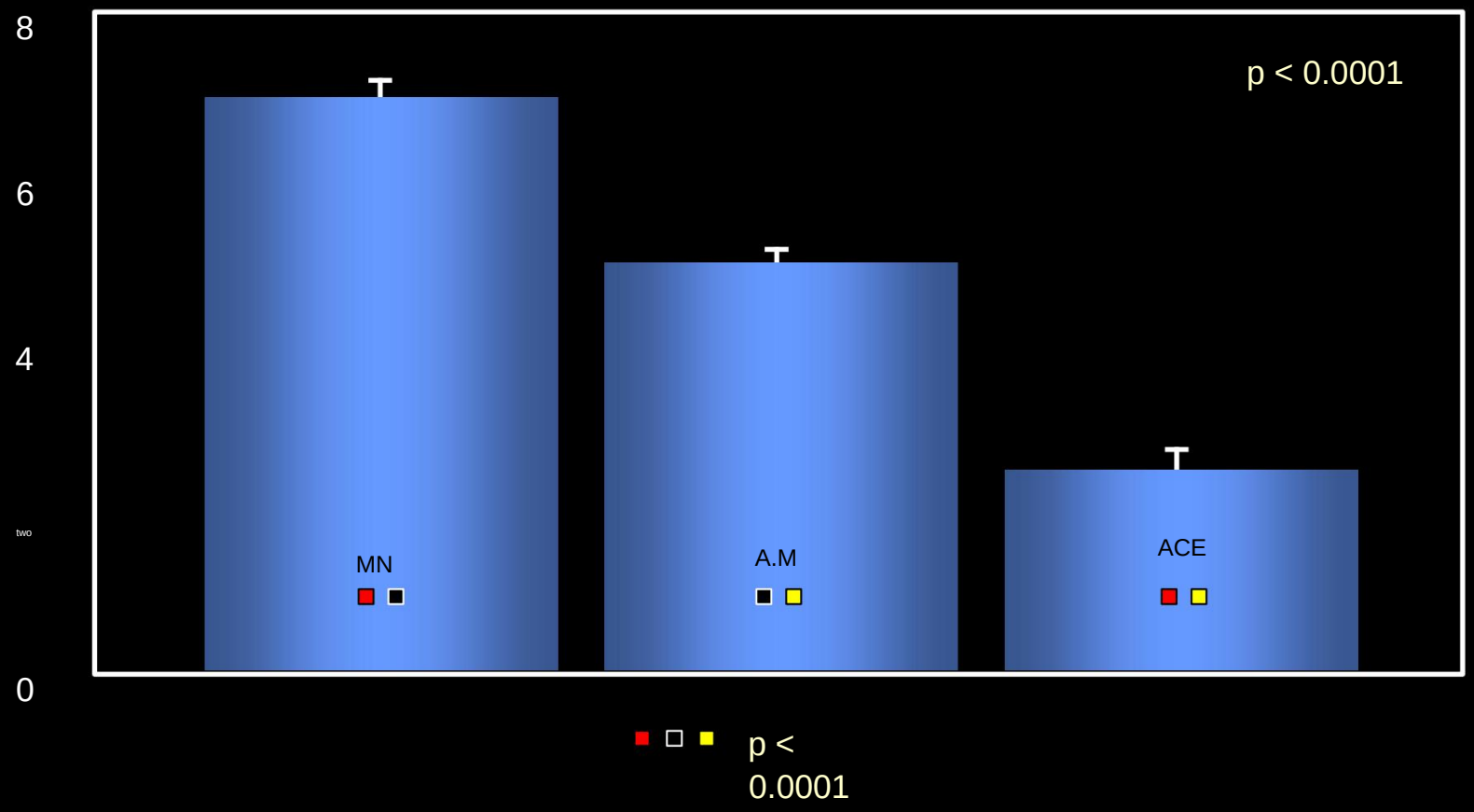
Vertical progression vs motility phenotypes



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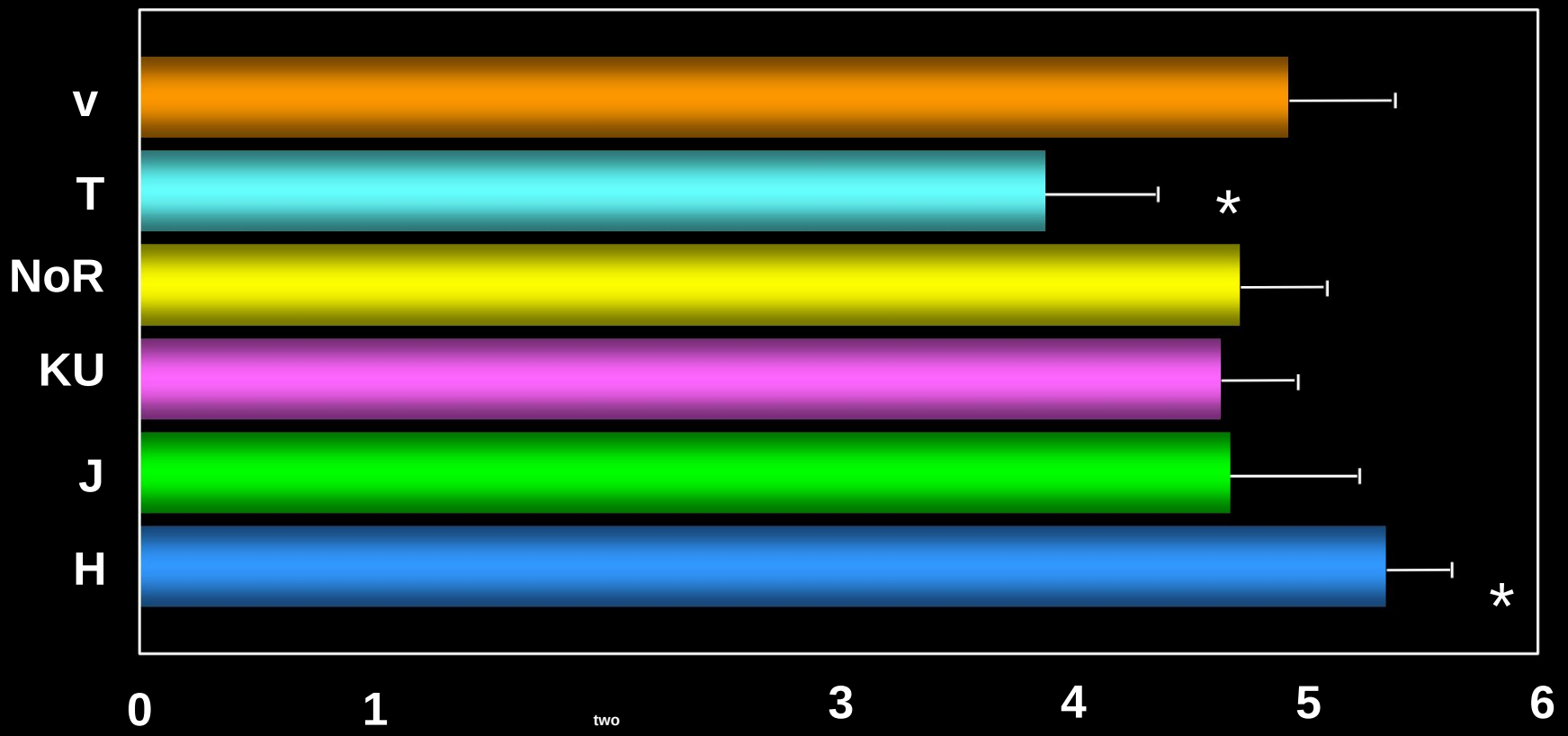
Mitochondrial haplogroups vs vertical progression



* ; p = 0.0287

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CONCLUSIONS:

THERE IS ASSOCIATION BETWEEN THE HAPLOGROUPS

MITOCHONDRIAL AND SPERMATIC MOTILITY. THE

HAPLOGROUP H CONFERS RESISTANCE

TO ASTENOZOOSPERMIA.

HAPLOGROUP T CONFERS SUSCEPTIBILITY TO ASTENOZOOSPERMIA.

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CONCLUSIONS:

THE CUBAN T HAPLOGROUP IS REPRESENTATIVE OF THE AFRICAN AMERICAN HAPLOGROUP T.

IT IS THE ASSEMBLY OF THE HAPLOGROUP T, AND NOT A BRANCH PARTICULARLY, THE ONE ASSOCIATED WITH ASTENOZOOSPERMIA MODERATE.

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CONCLUSIONS:

THE DISTRIBUTION OF MITOCHONDRIAL HAPLOGROUPS IN THE

THE CUBAN POPULATION IS REPRESENTATIVE OF THE POPULATION

GENERAL AFRICAN AMERICAN.

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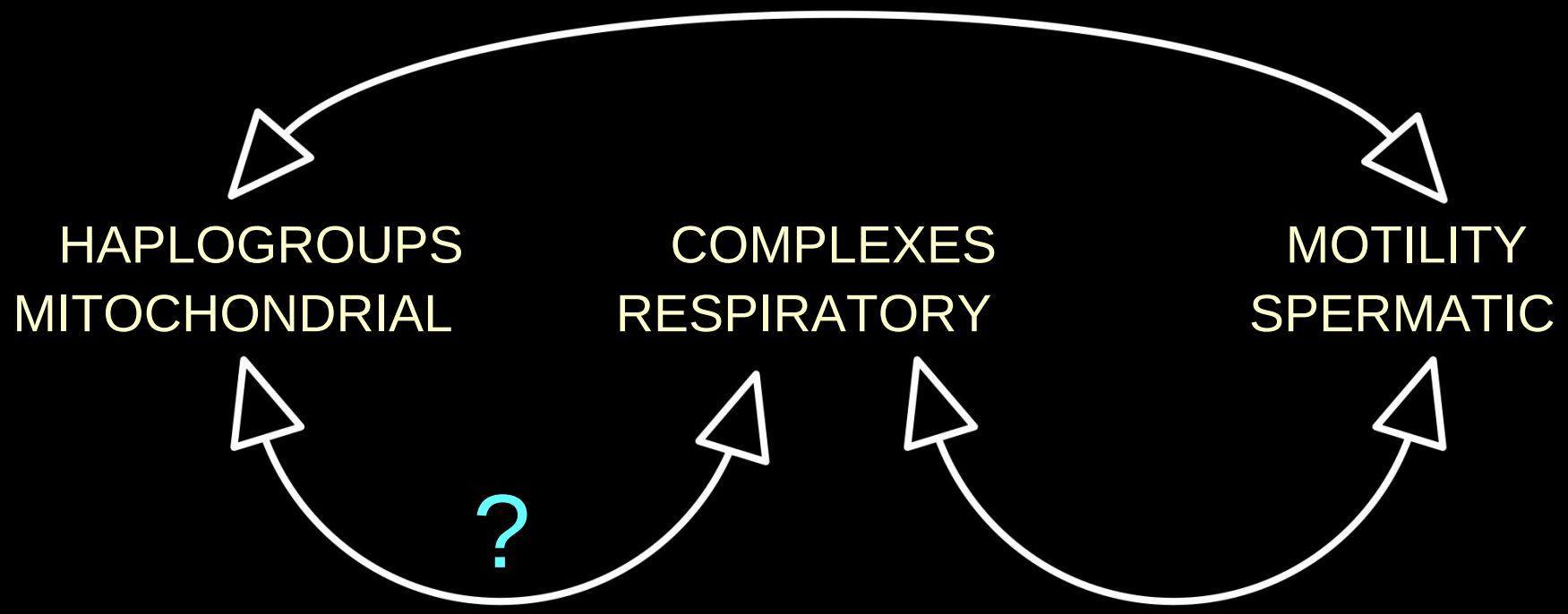
Study of the biochemical phenotype



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CONCLUSIONS:

IN THE 68 PATIENTS WITH DIFFERENT DEGREES OF VARICOCELE:

-THE ASSOCIATION BETWEEN mitochondrial DNA AND THE SPERM MOTILITY.

- THE BIOCHEMICAL PHENOTYPE ASSOCIATED WITH MOTILITY SPERMATIC TO THE MITOCHONDRIAL GENETIC BACKGROUND IS THE RESPIRATORY FUNCTION.

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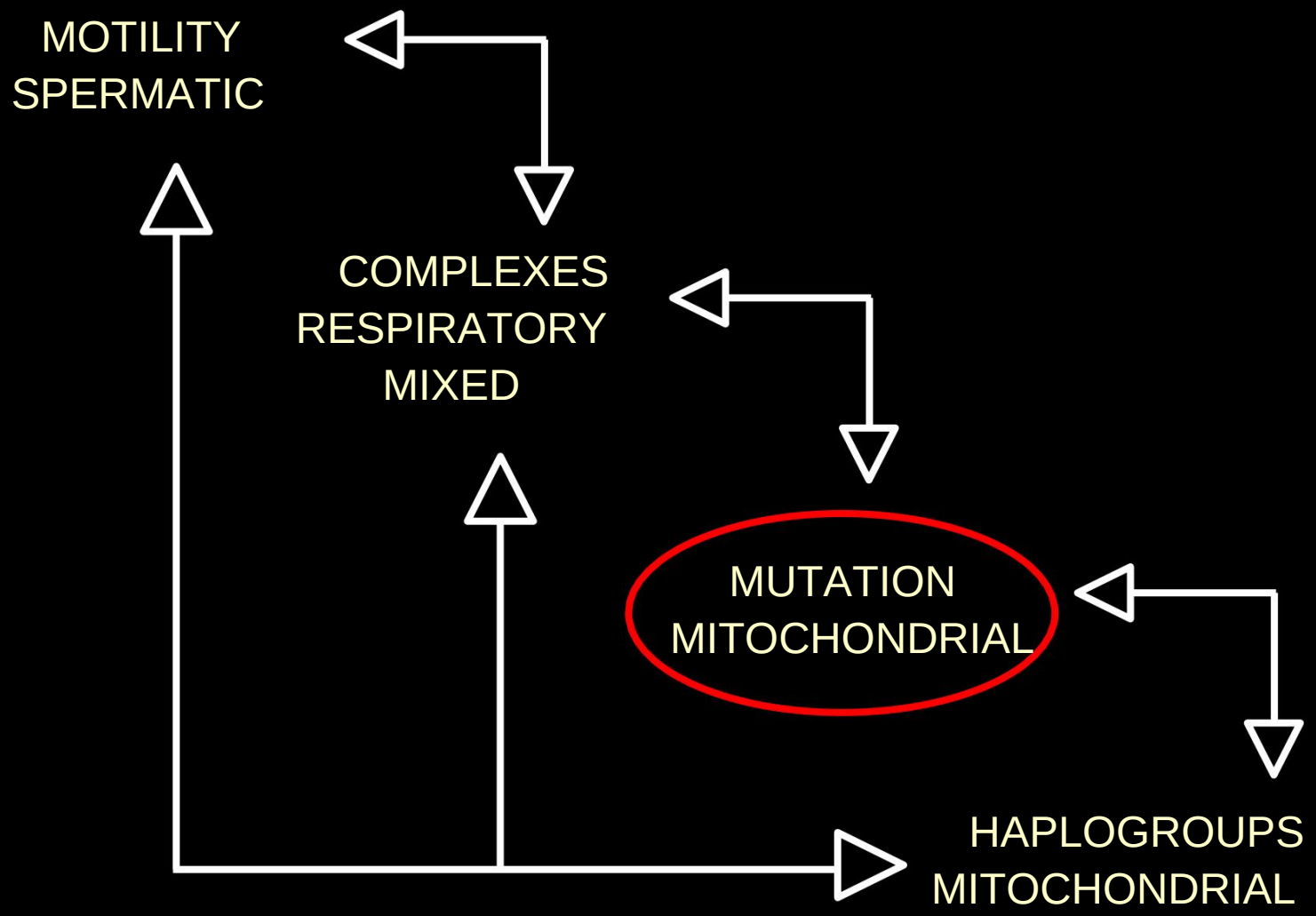
Study of the molecular phenotype



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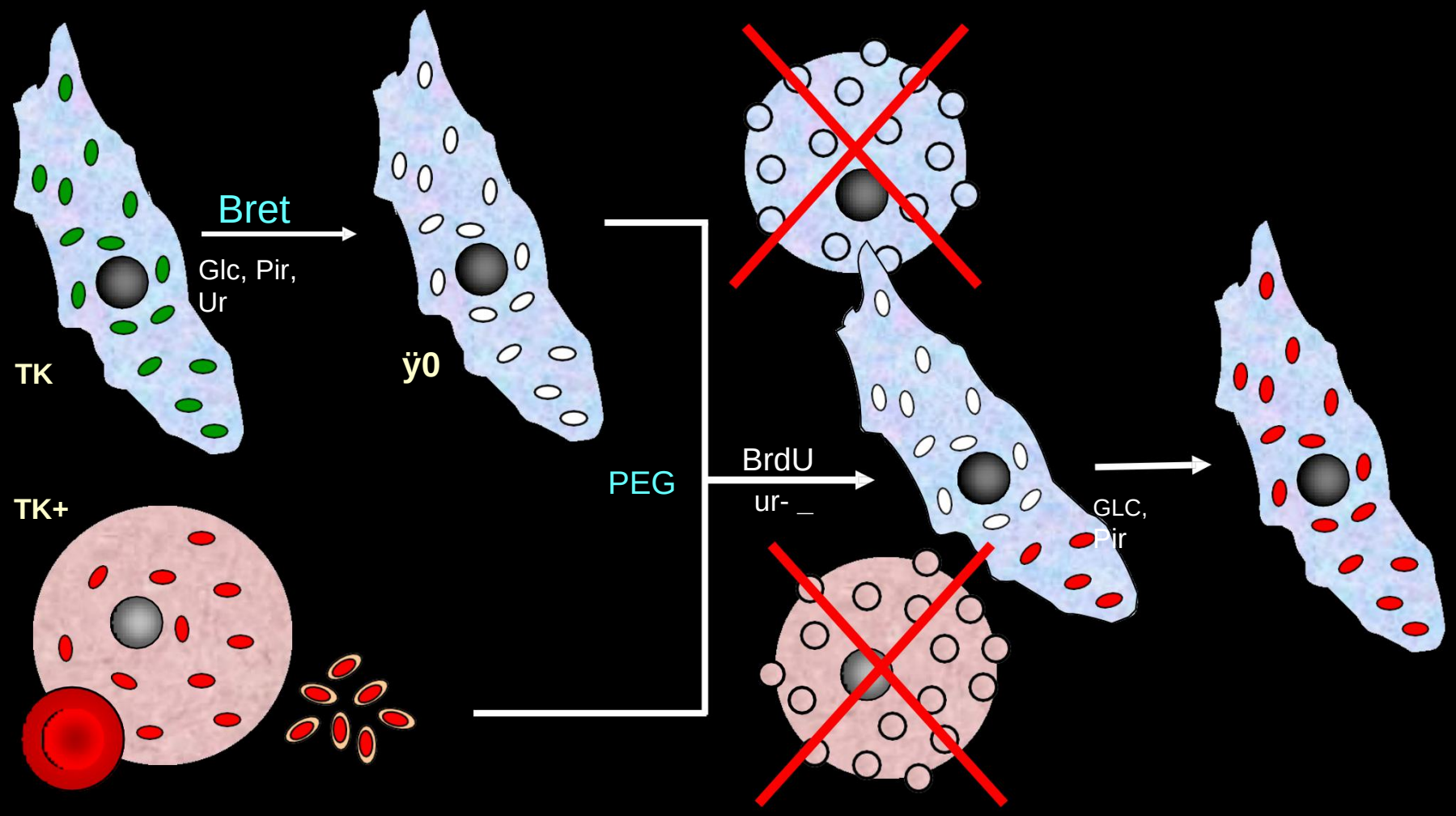
cybrids



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stress conditions

CONDITION	TEMPERATURE	FONT ENERGY
BASAL	37ºC	GLUCOSE
LOW STRESS	35ºC	GLUCOSE
MODERATE STRESS	37ºC	GALACTOSE
SEVERE STRESS	35ºC	GALACTOSE

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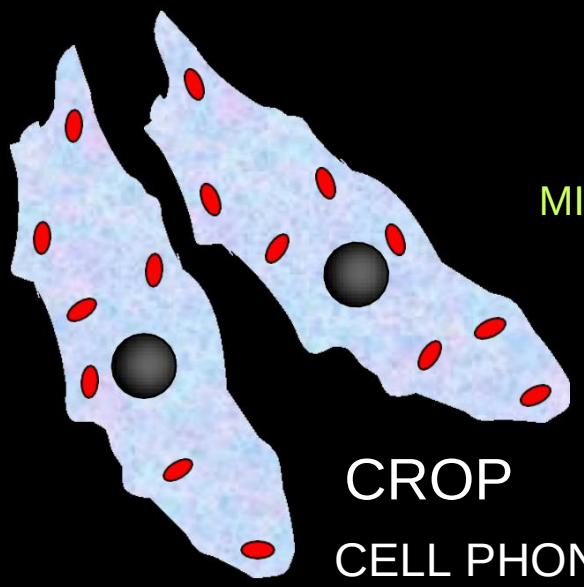
FACULTAD DE CIENCIAS MÉDICAS
"MIGUEL ENRÍQUEZ"

Stress and mitochondrial biogenesis

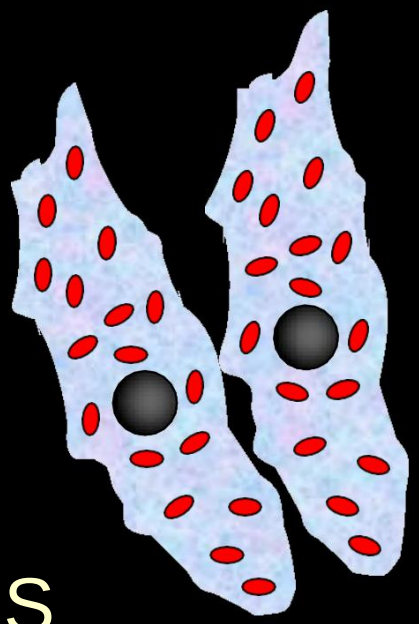


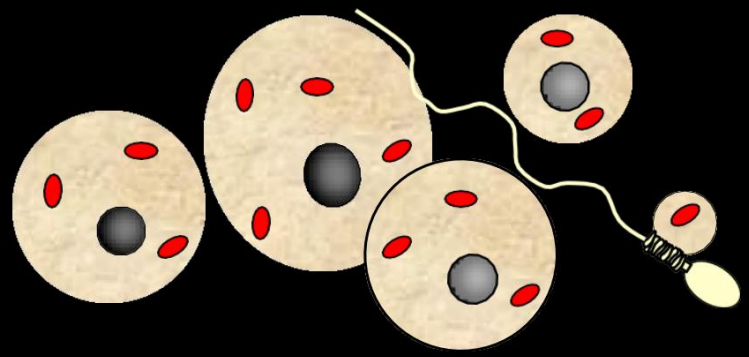
CROP
CELL PHONE

BIOGENESIS
MITOCHONDRIAL

EXPERIMENTAL

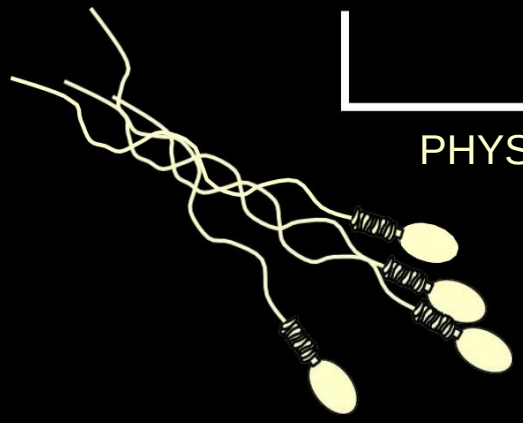
STRESS





SPERMATOGENESIS

PHYSIOLOGICAL



NO
BIOGENESIS
MITOCHONDRIAL

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RECOMMENDATIONS.

-We suggest that varicocele repair be performed in patients who have high mitochondrial DNA fragmentation associated with male infertility in their semen samples prior to surgery.

- An annual control with ultrasound of the testicular volume is recommended, since it is the most precise and reproducible method to measure the variations in the size of the testicle.

-Variations of more than 2 ml or 20% of the volume by ultrasound is currently the best indicator of testicular damage.

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